Office de la Propriété Intellectuelle du Canada
Un organisme d'Industrie Canada

Canadian Intellectual Property Office
An agency of Industry Canada

CA 2432350 A1 2002/07/18

(21) 2 432 350

(12) DEMANDE DE BREVET CANADIEN
CANADIAN PATENT APPLICATION

(13) A1

(86) Date de dépôt PCT/PCT Filing Date: 2002/01/09
(87) Date publication PCT/PCT Publication Date: 2002/07/18
(85) Entrée phase nationale/National Entry: 2003/06/30
(86) N° demande PCT/PCT Application No.: EP 2002/000152
(87) N° publication PCT/PCT Publication No.: 2002/055693
(30) Priorités/Priorities: 2001/01/09 (101 00 586.5) DE;
2001/10/26 (101 55 280.7) DE;
2001/11/29 (101 58 411.3) DE;
2001/12/07 (101 60 151.4) DE

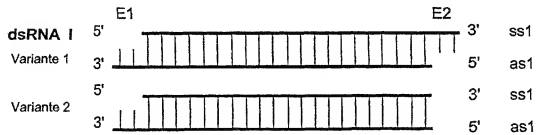
(51) Cl.Int.^{7}/Int.Cl.^{7} C12N 15/11, A61K 31/713, A61P 35/00, C12N 15/88

(71) Demandeur/Applicant:
RIBOPHARMA AG, DE

(72) Inventeurs/Inventors:
KREUTZER, ROLAND, DE;
LIMMER, STEPHAN, DE;
ROST, SYLVIA, DE;
HADWIGER, PHILIPP, DE

(74) Agent: AIKINS, MACAULAY & THORVALDSON

(54) Titre : PROCEDE POUR INHIBER L'EXPRESSION D'UN GENE CIBLE
(54) Title: METHOD FOR INHIBITING THE EXPRESSION OF A TARGET GENE



(57) Abrégé/Abstract:
The invention relates to a method for inhibiting the expression of a target gene in a cell, comprising the following steps: introduction of an amount of at least one dual-stranded ribonucleic acid (dsRNA I) which is sufficient to inhibit the expression of the target gene. The dsRNA I has a dual-stranded structure formed by a maximum of 49 successive nucleotide pairs. One strand (as1) or at least one section of the one strand (as1) of the dual-stranded structure is complementary to the sense strand of the target gene. The dsRNA has an overhang on the end (E1) of dsRNA I formed by 1 - 4 nucleotides.

(12) NACH DEM VERTRAG ÜBER DIE INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT) VERÖFFENTLICHTE INTERNATIONALE ANMELDUNG

(19) Weltorganisation für geistiges Eigentum
Internationales Büro

(43) Internationales Veröffentlichungsdatum
18. Juli 2002 (18.07.2002)

PCT

(10) Internationale Veröffentlichungsnummer
WO 02/055693 A2

(51) Internationale Patentklassifikation[7]: C12N 15/11

(21) Internationales Aktenzeichen: PCT/EP02/00152

(22) Internationales Anmeldedatum:
9. Januar 2002 (09.01.2002)

(25) Einreichungssprache: Deutsch

(26) Veröffentlichungssprache: Deutsch

(30) Angaben zur Priorität:

101 00 586.5	9. Januar 2001 (09.01.2001)	DE
101 55 280.7	26. Oktober 2001 (26.10.2001)	DE
101 58 411.3	29. November 2001 (29.11.2001)	DE
101 60 151.4	7. Dezember 2001 (07.12.2001)	DE

(71) Anmelder *(für alle Bestimmungsstaaten mit Ausnahme von US)*: **RIBOPHARMA AG** [DE/DE]; Universitätsstrasse 30, 95447 Bayreuth (DE).

(72) Erfinder; und

(75) Erfinder/Anmelder *(nur für US)*: **KREUTZER, Roland** [DE/DE]; Universitätsstrasse 30, 95447 Bayreuth (DE). **LIMMER, Stephan** [DE/DE]; Universitätsstrasse 30, 95447 Bayreuth (DE). **ROST, Sylvia** [DE/DE]; Universitätsstrasse 30, 95447 Bayreuth (DE). **HADWIGER, Philipp** [DE/DE]; Universitätsstrasse 30, 95447 Bayreuth (DE).

(74) Anwalt: **GASSNER, Wolfgang**; Nägelsbachstrasse 49a, 91052 Erlangen (DE).

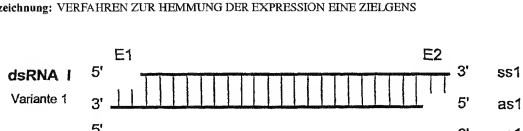
(81) Bestimmungsstaaten *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Bestimmungsstaaten *(regional)*: ARIPO-Patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), eurasisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI-Patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

[Fortsetzung auf der nächsten Seite]

(54) Title: METHOD FOR INHIBITING THE EXPRESSION OF A TARGET GENE

(54) Bezeichnung: VERFAHREN ZUR HEMMUNG DER EXPRESSION EINE ZIELGENS



(57) Abstract: The invention relates to a method for inhibiting the expression of a target gene in a cell, comprising the following steps: introduction of an amount of at least one dual-stranded ribonucleic acid (dsRNA I) which is sufficient to inhibit the expression of the target gene. The dsRNA I has a dual-stranded structure formed by a maximum of 49 successive nucleotide pairs. One strand (as1) or at least one section of the one strand (as1) of the dual-stranded structure is complementary to the sense strand of the target gene. The dsRNA has an overhang on the end (E1) of dsRNA I formed by 1 - 4 nucleotides.

(57) Zusammenfassung: Die Erfindung betrifft ein Verfahren zur Hemmung der Expression eines Zielgens in einer Zelle umfassend die folgenden Schritte: Einführen mindestens einer doppelsträngigen Ribonukleinsäure (dsRNA I) in einer zur Hemmung der Expression des Zielgens ausreichenden Menge, wobei die dsRNA I eine doppelsträngige aus höchstens 49 aufeinanderfolgenden Nukleotidpaaren gebildete Struktur aufweist, und wobei ein Strang (as1) oder zumindest ein Abschnitt des einen Strangs (as1) der doppelsträngigen Struktur komplementär zum Sinn-Strang des Zielgens ist, und wobei die dsRNA am einen Ende (E1) der dsRNA I einen aus 1 bis 4 Nukeotiden gebildeten überhang aufweist.

WO 02/055693 A2

Veröffentlicht:

— *ohne internationalen Recherchenbericht und erneut zu veröffentlichen nach Erhalt des Berichts*

Zur Erklärung der Zweibuchstaben-Codes und der anderen Abkürzungen wird auf die Erklärungen ("Guidance Notes on Codes and Abbreviations") am Anfang jeder regulären Ausgabe der PCT-Gazette verwiesen.

Patent Claims

1. Method for inhibiting the expression of a target gene in a cell, comprising the following steps:

Introduction of at least one double-stranded ribonucleic acid (dsRNA I) in a quantity sufficient to inhibit expression of the target gene,

whereby dsRNA I exhibits a double-stranded structure consisting of a maximum of 49 successive nucleotide pairs, and whereby one strand (as1) or at least one segment of the strand (as1) of the double-stranded structure is complementary to the target gene,

and whereby at least one end (E1, E2) of dsRNA I exhibits an overhang consisting of 1 to 4 nucleotides.

2. Method in accordance with Claim 1, whereby dsRNA I exhibits the overhang at the 3'-end of one strand (as1) and/or at the 3'-end of the other strand (ss1).

3. Method in accordance with Claim 1 or 2, whereby dsRNA I has a smooth configuration at one end (E1, E2).

4. Method in accordance with Claim 3, whereby the smooth end (E1, E2) contains the 5'-end of one strand (as1).

5. Method in accordance with one of the preceding claims, whereby the overhang consists of 1 to 4 nucleotides, preferably of 1 or 2 nucleotides.

6. Method in accordance with one of the preceding claims, whereby at least one further double-stranded ribonucleic

acid (dsRNA II) having a configuration according to the dsRNA I as defined in the preceding claims, is introduced into the cell, whereby one strand (as1) of dsRNA I is complementary to a first region (B1) of the target gene, and whereby another strand (as2) or at least one segment of the other strand (as2) of dsRNA II is complementary to a second region (B2) of the target gene.

7. Method in accordance with one of the preceding claims, whereby dsRNA I and/or dsRNA II exhibits a length of fewer than 25 successive nucleotide pairs, preferably 19 to 23.

8. Method in accordance with one of the preceding claims, whereby the first (B1) and the second (B2) region overlap segmentally or adjoin each other.

9. Method in accordance with one of the preceding claims, whereby the first (B1) and the second (B2) region are separated from each other.

10. Method in accordance with one of the preceding claims, whereby the target gene exhibits one of the sequences SQ001 to SQ140.

11. Method in accordance with one of the preceding claims, whereby the target gene is selected from the following group: oncogene, cytokine gene, Id protein gene, prion gene, genes from angiogenesis-inducing molecules, from adhesion molecules, and from cell-surface receptors; genes from proteins that are involved in metastatic and/or invasive

processes; genes from proteinases as well as molecules that regulate apoptosis and the cell cycle.

12. Method in accordance with one of the preceding claims, whereby the target gene is the MDR1 gene.

13. Method in accordance with one of the preceding claims, whereby one of the sequences SQ141-173 or a dsRNA construct being combined of two antisense- (as1/2) and sense sequences (ss1/2) belonging together and belonging to sequences SQ141-173 are used as the dsRNA I/II.

14. Method in accordance with one of the preceding claims, whereby expression is inhibited according to the principle of RNA interference.

15. Method in accordance with one of the preceding claims, whereby the target gene is expressed in pathogenic organisms, preferably in plasmodia.

16. Method in accordance with one of the preceding claims, whereby the target gene is a component of a virus or viroid.

17. Method in accordance with Claim 16, whereby the virus is a human pathogenic virus or viroid.

18. Method in accordance with Claim 16, whereby the virus or viroid is a virus or viroid that is pathogenic in animals or plants.

19. Method in accordance with one of the preceding claims, whereby unpaired nucleotides are substituted by nucleoside thiophosphates.

20. Method in accordance with one of the preceding claims, whereby at least one end (E1, E2) of dsRNA I/II is modified

in order to counter decomposition in the cell or dissociation in the individual strands.

21. Method in accordance with one of the preceding claims, whereby the cohesion of the double-stranded structure effected by the complementary nucleotide pairs is increased by at least one chemical bond.

22. Method in accordance with one of the preceding claims, whereby the chemical link is achieved either by a covalent or ionic bond, a hydrogen bond, hydrophobic interaction, preferably by means of van der Waals or stacking interactions, or by means of metal-ion coordination.

23. Method in accordance with one of the preceding claims, whereby the chemical link is formed in the vicinity of one end (E1, E2).

24. Method in accordance with one of the preceding claims, whereby the chemical link is created by one or several linkage groups, whereby the linkage groups are preferably poly-(oxyphosphinico-oxy-1,3-propandiol) and/or oligoethyleneglycol chains.

25. Method in accordance with one of the preceding claims, whereby the chemical link is formed by using branched nucleotide analogs instead of nucleotides.

26. Method in accordance with one of the preceding claims, whereby the chemical link is formed by purine analogs.

27. Method in accordance with one of the preceding claims, whereby the chemical link is formed by azabenzene units.

28. Method in accordance with one of the preceding claims, whereby at least one of the following groups is used in creating the chemical link: methylene blue; bifunctional groups, preferably bis-(2-chlorethyl)-amine; N-acetyl-N'-(p-glyoxyl-benzoyl)-cystamine; 4-thiouracil; psoralen.

29. Method in accordance with one of the preceding claims, whereby the chemical link is formed by thiophosphoryl groups that are attached in the vicinity of the ends (E1, E2) of the double-stranded region.

30. Method in accordance with one of the preceding claims, whereby the chemical link is formed by triple helix bonds that are present in the vicinity of the ends (E1, E2).

31. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is enclosed in micellar structures, most advantageously in liposomes.

32. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is bound to, associated with, or enclosed by at least one viral case protein that stems from a virus, is derived from it, or is synthetically produced.

33. Method in accordance with one of the preceding claims, whereby the coat protein is derived from polyomavirus.

34. Method in accordance with one of the preceding claims, whereby the coat protein contains Virus Protein 1 (VP1) and/or Virus Protein 2 (VP2) of the polyomavirus.

35. Method in accordance with one of the preceding claims, whereby at the formation of a capsid or capsid-like

structure, the one side is turned toward the inside of the capsid or capsid-like structure.

36. Method in accordance with one of the preceding claims, whereby the one strand (as1, as2) of dsRNA I/II is complementary to the primary or processed RNA transcript of the target gene.

37. Method in accordance with one of the preceding claims, whereby the cell is a vertebrate cell or a human cell.

38. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is administered to a mammal at a maximum dosage of 5 mg/kg body weight per day, preferably to a human.

39. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is mixed in a buffer solution for application.

40. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is administered orally or by intravenous, intratumoral, or intraperitoneal injection or infusion, or by inhalation.

41. Use of a double-stranded ribonucleic acid (dsRNA I) for inhibiting the expression of the target gene in a cell, whereby dsRNA I exhibits a double-stranded structure consisting of a maximum of 49 successive nucleotide pairs, and whereby one strand (as1) or at least one segment of a strand (as1) of the double-stranded structure is complementary to the target gene,

and whereby dsRNA I exhibits an overhang consisting of 1 to 4 nucleotides at at least one end (E1, E2).

42. Use in accordance with Claim 41, whereby dsRNA I exhibits the overhang at the 3'-end of one strand (as1) and/or at the 3'-end of the other strand (ss1).

43. Use in accordance with Claim 41 or 42, whereby dsRNA I has a smooth configuration at one end (E1, E2).

44. Use in accordance with Claim 43, whereby the smooth end (E1, E2) contains the 5'-end of one strand (as1).

45. Use in accordance with one of the Claims 41 to 44, whereby the overhang consists of 1 to 4 nucleotides, preferably of 1 or 2 nucleotides.

46. Use in accordance with Claims 41 to 45, whereby at least one further double-stranded ribonucleic acid (dsRNA II) having a configuration according to dsRNA I as defined in claims 41 to 45, is introduced into the cell, whereby the one strand (as1) or at least one segment of the strand (as1) of the double-stranded structure of the dsRNA I is complementary to a first region (B1) of the sense strand of the target gene, and whereby the other strand (as2) or at least one segment of the other strand (as2) of the double-stranded structure of dsRNA II is complementary to a second region (B2) of the target gene.

47. Use in accordance with one of the Claims 41 to 46, whereby the dsRNA I and/or dsRNA II exhibits a length of fewer than 25, preferably 19 to 23, successive nucleotide pairs.

48. Use in accordance with one of the Claims 41 to 47, whereby the first (B1) and second region (B2) overlap segmentally or adjoin each other.

49. Use in accordance with one of the Claims 41 to 48, whereby the first (B1) and second region (B2) are separated from each other.

50. Use in accordance with one of the Claims 41 to 49, whereby the target gene exhibits one of the sequences SQ001 to SQ140.

51. Use in accordance with one of the Claims 41 to 50, whereby the target gene is selected from the following group: oncogene, cytokine gene, Id protein gene, prion gene, genes from angiogenesis-inducing molecules, from adhesion molecules, and from cell-surface receptors; genes from proteins that are involved in metastatic and/or invasive processes; genes from proteinases as well as molecules that regulate apoptosis and the cell cycle.

52. Use in accordance with one of the Claims 41 to 51, whereby the target gene is the MRD1 gene.

53. Use in accordance with one of the Claims 41 to 52, whereby one of the sequences SQ141-173 or a dsRNA construct being combined of two antisense- (as1/2) and sense sequences (ss1/2) belonging together and belonging to sequences SQ141-173 are used as the dsRNA I/II.

54. Use in accordance with one of the Claims 41 to 53, whereby expression is inhibited according to the principal of RNA interference.

55. Use in accordance with one of the Claims 41 to 54, whereby the target gene is expressed in pathogenic organisms, preferably in plasmodia.

56. Use in accordance with one of the Claims 41 to 55, whereby the target gene is a component of a virus or viroid.

57. Use in accordance with Claim the 56, whereby the virus is a human pathogenic virus or viroid.

58. Use in accordance with claim 56, whereby the virus or viroid is a virus or viroid that is pathogenic in animals or plants.

59. Use in accordance with one of the Claims 41 to 58, whereby unpaired nucleotides are substituted by nucleoside thiophosphates.

60. Use in accordance with one of the Claims 41 to 59, whereby at least one end (E1, E2) of the dsRNA is modified in order to counter decomposition in the cell or dissociation in the individual strands.

61. Use in accordance with one of the Claims 41 to 60, whereby the cohesion of the double-stranded structure effected by the complementary nucleotide pairs is increased by at least one chemical bond.

62. Use in accordance with one of the Claims 41 to 61, whereby the chemical link is achieved either by a covalent or ionic bond, a hydrogen bond, hydrophobic interaction, preferably by means of van der Waals or stacking interactions, or by means of metal-ion coordination.

63. Use in accordance with one of the Claims 41 to 62, whereby the chemical link is formed in the vicinity of one end (E1, E2).

64. Use in accordance with one of the Claims 41 to 63, whereby the chemical link is created by one or several linkage groups, whereby the linkage groups are preferably poly-(oxyphosphinico-oxy-1,3-propandiol) and/or oligoethyleneglycol chains.

65. Use in accordance with one of the Claims 41 to 64, whereby the chemical link is formed by using branched nucleotide analogs instead of nucleotides.

66. Use in accordance with one of the Claims 41 to 65, whereby the chemical link is formed by purine analogs.

67. Use in accordance with one of the Claims 41 to 66, whereby the chemical link is formed by azabenzene units.

68. Use in accordance with one of the Claims 41 to 67, whereby at least one of the following groups is used in creating the chemical link: methylene blue; bifunctional groups, preferably bis-(2-chlorethyl)-amine; N-acetyl-N'-(p-glyoxyl-benzoyl)-cystamine; 4-thiouracil; psoralen.

69. Use in accordance with one of the Claims 41 to 68, whereby the chemical link is formed by thiophosphoryl groups that are attached in the vicinity of the ends (E1, E2) of the double-stranded region.

70. Use in accordance with one of the Claims 41 to 69, whereby the link is produced by triple helix bonds present in the vicinity of the ends (E1, E2).

71. Use in accordance with one of the Claims 41 to 70, whereby the dsRNA I/II is enclosed in micellar structures, most advantageously in liposomes.

72. Use in accordance with one of the Claims 41 to 71, whereby the dsRNA I/II is bound to, associated with, or enclosed by at least one viral case protein that stems from a virus, is derived from it, or is synthetically produced.

73. Use in accordance with one of the Claims 41 to 72, whereby the case protein is derived from polyomavirus.

74. Use in accordance with one of the Claims 41 to 73, whereby the case protein contains Virus Protein 1 (VP1) and/or Virus Protein 2 (VP2) of the polyomavirus.

75. Use in accordance with one of the Claims 41 to 74, whereby at the formation of a capsid or capsid-like structure, the one side is turned toward the inside of the capsid or capsid-like structure.

76. Use in accordance with one of the Claims 41 to 75, whereby the one strand (as1, as2) of dsRNA I/II is complementary to the primary or processed RNA transcript of the target gene.

77. Use in accordance with one of the Claims 41 to 76, whereby the cell is a vertebrate cell or a human cell.

78. Use in accordance with one of the Claims 41 to 77, whereby the dsRNA I/II is administered to a mammal at a maximum dosage of 5 mg/kg body weight per day, preferably to human being.

79. Use in accordance with one of the Claims 41 to 78, whereby the dsRNA I/II is mixed with a buffer solution for application.

80. Use in accordance with one of the Claims 41 to 79, whereby the dsRNA I/II is administered orally or by intravenous, intratumoral, or intraperitoneal injection or infusion, or by inhalation.

81. Medicament for inhibiting the expression of a target gene in a cell, containing a double-stranded ribonucleic acid (dsRNA I) in a dosage sufficient to inhibit the expression of the target gene,

whereby dsRNA I exhibits a double-stranded structure consisting of a maximum of 49 successive nucleotide pairs,

and whereby one strand (as1) or at least one segment of the strand (as1) of the double-stranded structure is complementary to the target gene,

and whereby at least one end (E1, E2) of the dsRNA I exhibits an overhang consisting of 1 to 4 nucleotides.

82. Medicament in accordance with Claim 81, whereby dsRNA I exhibits the overhang at the 3'-end of one strand (as1) and/or at the 3'-end of the other strand (ss1).

83. Medicament in accordance with Claim 81 or 82, whereby the dsRNA I has a smooth configuration at one end (E1, E2).

84. Medicament in accordance with Claim 83, whereby the smooth end (E1, E2) contains the 5'-end of the first strand (as1).

85. Medicament in accordance with Claims 81 to 84, whereby the overhang consists of 1 to 4 nucleotides, preferably of 1 or 2 nucleotides.

86. Medicament in accordance with one of the Claims 81 to 85, whereby at least one further double-stranded ribonucleic acid (dsRNA II) having a configuration according to the dsRNA I as defined in Claims 81 to 85, and whereby the one strand (as1) of dsRNA I is complementary to a first region (B1) of the target gene, and whereby another strand (as2) or at least one segment of the other strand (as2) of dsRNA II is complementary to a second region (B2) of the target gene.

87. Medicament in accordance with one of the Claims 81 to 86, whereby the dsRNA I and/or dsRNA II exhibits a length of fewer than 25, preferably in 19 to 23, successive nucleotide pairs.

88. Medicament in accordance with one of the Claims 81 to 87, whereby the first (B1) and the second region (B2) overlap segmentally or adjoin each other.

89. Medicament in accordance with one of the Claims 81 to 88, whereby the target gene exhibits one of the sequences SQ001 to SQ140.

90. Medicament in accordance with one of the Claims 81 to 89, whereby the target gene is selected from the following group: oncogene, cytokine gene, Id protein gene, prion gene, genes from angiogenesis-inducing molecules, from adhesion molecules, and from cell-surface receptors; genes from proteins that are involved in metastatic and/or invasive processes; genes from proteinases as well as molecules that regulate apoptosis and the cell cycle.

91. Medicament in accordance with one of the Claims 81 to 90, whereby the target gene is the MRD1 gene.

92. Medicament in accordance with one of the Claims 81 to 91, whereby one of the sequences SQ141-173 or a dsRNA construct being combined of two antisense- (as1/2) and sense sequences (ss1/2) belonging together and belonging to sequences SQ141-173 are used as the dsRNA I/II.

93. Medicament in accordance with one of the Claims 81 to 92, whereby expression is inhibited according to the principle of RNA interference.

94. Medicament in accordance with one of the Claims 81 to 93, whereby the target gene is expressed in pathogenic organisms, most advantageously in plasmodia.

95. Medicament in accordance with one of the Claims 81 to 94, whereby the target gene is a component of a virus or viroid.

96. Medicament in accordance with Claim 95, whereby the virus is a human pathogenic virus or viroid.

97. Medicament in accordance with Claim 95, whereby the virus or viroid is a virus or viroid that is pathogenic in animals or plants.

98. Medicament in accordance with one of the Claims 81 to 97, whereby unpaired nucleotides are substituted with nucleoside thiophosphates.

99. Medicament in accordance with one of the Claims 81 to 98, whereby at least one end (E1, E2) of dsRNA I/II is modified

in order to counter decomposition in the cell or dissociation in the individual strand.

100. Medicament in accordance with one of the Claims 81 to 99, whereby the cohesion of the double-stranded structure effected by the complementary nucleotide pairs is increased by at least one chemical bond.

101. Medicament in accordance with one of the Claims 81 to 100, whereby the chemical link is achieved either by a covalent or ionic bond, a hydrogen bond, hydrophobic interaction, preferably by means of van der Waals or stacking interactions, or by means of metal-ion coordination.

102. Medicament in accordance with one of the Claims 81 to 101, whereby the chemical link is formed in the vicinity of one end (E1, E2).

103. Medicament in accordance with one of the Claims 81 to 102, whereby the chemical link is created by one or several linkage groups, whereby the linkage groups are preferably poly-(oxyphosphinico-oxy-1,3-propandiol) and/or oligoethyleneglycol chains.

104. Medicament in accordance with one of the Claims 81 to 103, whereby the chemical link is formed by using branched nucleotide analogs instead of nucleotides.

105. Medicament in accordance with one of the Claims 81 to 104, whereby the chemical link is formed by purine analogs.

106. Medicament in accordance with one of the Claims 81 to 105, whereby the chemical link is formed by azabenzene units.

107. Medicament in accordance with one of the Claims 81 to 106, whereby at least one of the following groups is used in creating the chemical link: methylene blue; bifunctional groups, preferably bis-(2-chlorethyl)-amine; N-acetyl-N'-(p-glyoxyl-benzoyl)-cystamine; 4-thiouracil; psoralen.

108. Medicament in accordance with one of the Claims 81 to 107, whereby the chemical link is formed by thiophosphoryl groups that are attached in the vicinity of the ends (E1, E2) of the double-stranded region.

109. Medicament in accordance with one of the Claims 81 to 108, whereby the chemical link is formed by triple helix bonds that are present in the vicinity of the ends (E1, E2).

110. Medicament in accordance with one of the Claims 81 to 109, whereby the dsRNA I/II is enclosed in micellar structures, most advantageously in liposomes.

111. Medicament in accordance with one of the Claims 81 to 110, whereby the dsRNA I/II is bound to, associated with, or enclosed by at least one viral case protein that stems from a virus, is derived from it, or is synthetically produced.

112. Medicament in accordance with one of the Claims 81 to 111, whereby the coat protein is derived from polyomavirus.

113. Medicament in accordance with one of the Claims 81 to 112, whereby the coat protein contains Virus Protein 1 (VP1) and/or Virus Protein 2 (VP2) of the polyomavirus.

114. Medicament in accordance with one of the Claims 81 to 113, whereby at the formation of a capsid or capsid-like

structure, the one side is turned toward the inside of the capsid or capsid-like structure.

115. Medicament in accordance with one of the Claims 81 to 114, whereby the one strand (as1, as2) of dsRNA I/II is complementary to the primary or processed RNA transcript of the target gene.

116. Medicament in accordance with one of the Claims 81 to 115, whereby the cell is a vertebrate cell or a human cell.

117. Medicament in accordance with one of the Claims 81 to 116, whereby the first (B1) and the second region (B2) are separated from each other.

118. Medicament in accordance with one of the Claims 81 to 117, whereby the dsRNA is administered at a maximum amount of 5 mg per dose.

119. Medicament in accordance with one of the Claims 81 to 118, whereby the dsRNA is mixed in a buffer solution for application.

120. Medicament in accordance with one of the Claims 81 to 119, whereby the dsRNA is administered orally or by intravenous, intratumoral, or intraperitoneal injection or infusion, or by inhalation.

121. Method for inhibiting the expression of a target gene in a cell, comprising the following steps:

Introduction of at least one double-stranded ribonucleic acid (dsRNA I) in a quantity sufficient to inhibit expression of the target gene,

whereby dsRNA I exhibits a double-stranded structure consisting of a maximum of 49 successive nucleotide pairs, and whereby one strand (as1) or at least one segment of the strand (as1) of the double-stranded structure is complementary to the target gene,

and whereby at least one end (E1, E2) of the dsRNA I exhibits an overhang consisting of 1 to 4 nucleotides.

122. Method in accordance with Claim 1, whereby dsRNA I exhibits the overhang at the 3'-end of one strand (as1) and/or at the 3'-end of the other strand (ss1).

123. Method in accordance with Claim 1 or 2, whereby the dsRNA I has a smooth configuration at one end (E1, E2).

124. Method in accordance with Claim 3, whereby the smooth end (E1, E2) contains the 5'-end of one strand (as1).

125. Method in accordance with one of the preceding claims, whereby the overhang consists of 1 to 4 nucleotides, preferably of 1 or 2 nucleotides.

126. Method in accordance with one of the preceding claims, whereby at least one further double-stranded ribonucleic acid (dsRNA II) having a configuration according to the dsRNA I as defined in the preceding claims, is introduced into the cell, whereby the one strand (as1) of dsRNA I is complementary to a first region (B1) of the target gene, and whereby another strand (as2) or at least one segment of the other strand (as2) of dsRNA II is complementary to a second region (B2) of the target gene.

127. Method in accordance with one of the preceding claims, whereby the dsRNA I and/or dsRNA II exhibits a length of fewer than 25 successive nucleotide pairs, preferably 19 to 23.

128. Method in accordance with one of the preceding claims, whereby the first (B1) and the second (B2) region overlap segmentally or adjoin each other.

129. Method in accordance with one of the preceding claims, whereby the first (B1) and the second (B2) region are separated from each other.

130. Method in accordance with one of the preceding claims, whereby the target gene exhibits one of the sequences SQ001 to SQ140.

131. Method in accordance with one of the preceding claims, whereby the target gene is selected from the following group: oncogene, cytokine gene, Id protein gene, prion gene, genes from angiogenesis-inducing molecules, from adhesion molecules, and from cell-surface receptors; genes from proteins that are involved in metastatic and/or invasive processes; genes from proteinases as well as molecules that regulate apoptosis and the cell cycle.

132. Method in accordance with one of the preceding claims, whereby the target gene is the MDR1 gene.

133. Method in accordance with one of the preceding claims, whereby one of the sequences SQ141-173 or a dsRNA construct being combined of two antisense- (as1/2) and sense sequences (ss1/2) belonging together and belonging to sequences SQ141-173 are used as the dsRNA I/II.

134. Method in accordance with one of the preceding claims, whereby expression is inhibited according to the principle of RNA interference.

135. Method in accordance with one of the preceding claims, whereby the target gene is expressed in pathogenic organisms, preferably in plasmodia.

136. Method in accordance with one of the preceding claims, whereby the target gene is a component of a virus or viroid.

137. Method in accordance with Claim 16, whereby the virus is a human pathogenic virus or viroid.

138. Method in accordance with Claim 16, whereby the virus or viroid is a virus or viroid that is pathogenic in animals or plants.

139. Method in accordance with one of the preceding claims, whereby unpaired nucleotides are substituted by nucleoside thiophosphates.

140. Method in accordance with one of the preceding claims, whereby at least one end (E1, E2) of dsRNA I/II is modified in order to counter decomposition in the cell or dissociation in the individual strand.

141. Method in accordance with one of the preceding claims, whereby the cohesion of the double-stranded structure effected by the complementary nucleotide pairs is increased by at least one chemical bond.

142. Method in accordance with one of the preceding claims, whereby the chemical link is achieved either by a covalent or ionic bond, a hydrogen bond, hydrophobic interaction, preferably by means of van der Waals or stacking interactions, or by means of metal-ion coordination.

143. Method in accordance with one of the preceding claims, whereby the chemical link is formed in the vicinity of one end (E1, E2).

144. Method in accordance with one of the preceding claims, whereby the chemical link is created by one or several linkage groups, whereby the linkage groups are preferably poly-(oxyphosphinico-oxy-1,3-propandiol) and/or oligoethyleneglycol chains.

145. Method in accordance with one of the preceding claims, whereby the chemical link is formed by using branched nucleotide analogs instead of nucleotides.

146. Method in accordance with one of the preceding claims, whereby the chemical link is formed by purine analogs.

147. Method in accordance with one of the preceding claims, whereby the chemical link is formed by azabenzene units.

148. Method in accordance with one of the preceding claims, whereby at least one of the following groups is used in creating the chemical link: methylene blue; bifunctional groups, preferably bis-(2-chlorethyl)-amine; N-acetyl-N'-(p-glyoxyl-benzoyl)-cystamine; 4-thiouracil; psoralen.

149. Method in accordance with one of the preceding claims, whereby the chemical link is formed by thiophosphoryl groups

that are attached in the vicinity of the ends (E1, E2) of the double-stranded region.

150. Method in accordance with one of the preceding claims, whereby the chemical link is formed by triple helix bonds that are present in the vicinity of the ends (E1, E2).

151. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is enclosed in micellar structures, most advantageously in liposomes.

152. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is bound to, associated with, or enclosed by at least one viral case protein that stems from a virus, is derived from it, or is synthetically produced.

153. Method in accordance with one of the preceding claims, whereby the coat protein is derived from polyomavirus.

154. Method in accordance with one of the preceding claims, whereby the coat protein contains Virus Protein 1 (VP1) and/or Virus Protein 2 (VP2) of the polyomavirus.

155. Method in accordance with one of the preceding claims, whereby at the formation of a capsid or capsid-like structure, the one side is turned toward the inside of the capsid or capsid-like structure.

156. Method in accordance with one of the preceding claims, whereby the one strand (as1, as2) of dsRNA I/II is complementary to the primary or processed RNA transcript of the target gene.

157. Method in accordance with one of the preceding claims, whereby the cell is a vertebrate cell or a human cell.

158. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is administered to a mammal at a maximum dosage of 5 mg/kg body weight per day, preferably to human being.

159. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is mixed in a buffer solution for application.

160. Method in accordance with one of the preceding claims, whereby the dsRNA I/II is administered orally or by intravenous, intratumoral, or intraperitoneal injection or infusion, or by inhalation.

161. Use of a double-stranded ribonucleic acid (dsRNA I) for inhibiting the expression of the target gene in a cell, whereby dsRNA I exhibits a double-stranded structure consisting of a maximum of 49 successive nucleotide pairs, and whereby one strand (as1) or at least one segment of a strand (as1) of the double-stranded structure is complementary to the target gene, and whereby dsRNA I exhibits an overhang consisting of 1 to 4 nucleotides at at least one end (E1, E2).

162. Use in accordance with Claim 41, whereby dsRNA I exhibits the overhang at the 3'-end of one strand (as1) and/or at the 3'-end of the other strand (ss1).

163. Use in accordance with Claim 41 or 42, whereby the dsRNA I has a smooth configuration at one end (E1, E2).

164. Use in accordance with Claim 43, whereby the smooth end(E1, E2) contains the 5'-end of one strand (as1).

165. Use in accordance with one of the Claims 41 to 44, whereby the overhang consists of 1 to 4 nucleotides, preferably of 1 or 2 nucleotides.

166. Use in accordance with Claims 41 to 45, whereby at least one further double-stranded ribonucleic acid (dsRNA II), having a configuration according to the dsRNA I as defined in the preceding claims 41 to 45, is introduced into the cell, whereby the one strand (as1) or at least one segment of the strand (as1) of the double-stranded structure of the dsRNA I is complementary to a first region (B1) of the sense strand of the target gene, and whereby the other strand (as2) or at least one segment of the other strand (as2) of the double-stranded structure of dsRNA II is complementary to a second region (B2) of the target gene.

167. Use in accordance with one of the Claims 41 to 47, whereby the dsRNA I and/or dsRNA II exhibits a length of fewer than 25, preferably 19 to 23, successive nucleotide pairs.

168. Use in accordance with one of the Claims 41 to 47, whereby the first (B1) and second region (B2) overlap segmentally or adjoin each other.

169. Use in accordance with one of the Claims 41 to 48, whereby the first (B1) and second region (B2) are separated from each other.

170. Use in accordance with one of the Claims 41 to 49, whereby the target gene exhibits one of the sequences SQ001 to SQ140.

171. Use in accordance with one of the Claims 41 to 50, whereby the target gene is selected from the following group: oncogene, cytokine gene, Id protein gene, prion gene, genes from angiogenesis-inducing molecules, from adhesion molecules, and from cell-surface receptors; genes from proteins that are involved in metastatic and/or invasive processes; genes from proteinases as well as molecules that regulate apoptosis and the cell cycle.

172. Use in accordance with one of the Claims 41 to 51, whereby the target gene is the MRD1 gene.

173. Use in accordance with one of the Claims 41 to 52, whereby one of the sequences SQ141-173 or a dsRNA construct being combined of two antisense- (as1/2) and sense sequences (ss1/2) belonging together and belonging to sequences SQ141-173 are used as the dsRNA I/II.

174. Use in accordance with one of the Claims 41 to 53, whereby expression is inhibited according to the principal of RNA interference.

175. Use in accordance with one of the Claims 41 to 54, whereby the target gene is expressed in pathogenic organisms, preferably in plasmodia.

176. Use in accordance with one of the Claims 41 to 55, whereby the target gene is a component of a virus or viroid.

177. Use in accordance with Claim 56, whereby the virus is a human pathogenic virus or viroid.

178. Use in accordance with Claim 56 whereby the virus or viroid is a virus or viroid that is pathogenic in animals or plants.

179. Use in accordance with one of the Claims 41 to 58, whereby unpaired nucleotides are substituted by nucleoside thiophosphates.

180. Use in accordance with one of the Claims 41 to 59, whereby at least one end (E1, E2) of the dsRNA is modified in order to counter decomposition in the cell or dissociation in the individual strand.

181. Use in accordance with one of the Claims 41 to 60, whereby the cohesion of the double-stranded structure effected by the complementary nucleotide pairs is increased by at least one chemical bond.

182. Use in accordance with one of the Claims 41 to 61, whereby the chemical link is achieved either by a covalent or ionic bond, a hydrogen bond, hydrophobic interaction, preferably by means of van der Waals or stacking interactions, or by means of metal-ion coordination.

183. Use in accordance with one of the Claims 41 to 62, whereby the chemical link is formed in the vicinity of one end (E1, E2).

184. Use in accordance with one of the Claims 41 to 63, whereby the chemical link is created by one or several linkage groups, whereby the linkage groups are preferably poly-(oxyphosphinico-oxy-1,3-propandiol) and/or oligoethyleneglycol chains.

185. Use in accordance with one of the Claims 41 to 64, whereby the chemical link is formed by using branched nucleotide analogs instead of nucleotides.

186. Use in accordance with one of the Claims 41 to 65, whereby the chemical link is formed by purine analogs.

187. Use in accordance with one of the Claims 41 to 66, whereby the chemical link is formed by azabenzene units.

188. Use in accordance with one of the Claims 41 to 67, whereby at least one of the following groups is used in creating the chemical link: methylene blue; bifunctional groups, preferably bis-(2-chlorethyl)-amine; N-acetyl-N'-(p-glyoxyl-benzoyl)-cystamine; 4-thiouracil; psoralen.

189. Use in accordance with one of the Claims 41 to 68, whereby the chemical link is formed by thiophosphoryl groups that are attached in the vicinity of the ends (E1, E2) of the double-stranded region.

190. Use in accordance with one of the Claims 41 to 69, whereby the link is produced by triple helix bonds present in the vicinity of the ends (E1, E2).

191. Use in accordance with one of the Claims 41 to 70, whereby the dsRNA I/II is enclosed in micellar structures, most advantageously in liposomes.

192. Use in accordance with one of the Claims 41 to 71, whereby the dsRNA I/II is bound to, associated with, or enclosed by at least one viral case protein that stems from a virus, is derived from it, or is synthetically produced.

193. Use in accordance with one of the Claims 41 to 72, whereby the case protein is derived from polyomavirus.

194. Use in accordance with one of the Claims 41 to 73, whereby the case protein contains Virus Protein 1 (VP1) and/or Virus Protein 2 (VP2) of the polyomavirus.

195. Use in accordance with one of the Claims 41 to 74, whereby at the formation of a capsid or capsid-like structure, the one side is turned toward the inside of the capsid or capsid-like structure.

196. Use in accordance with one of the Claims 41 to 75, whereby the one strand (as1, as2) of dsRNA I/II is complementary to the primary or processed RNA transcript of the target gene.

197. Use in accordance with one of the Claims 41 to 76, whereby the cell is a vertebrate cell or a human cell.

198. Use in accordance with one of the Claims 41 to 77, whereby the dsRNA I/II is administered to a mammal at a maximum dosage of 5 mg/kg body weight per day, preferably to human being.

199. Use in accordance with one of the Claims 41 to 78, whereby the dsRNA I/II is mixed with a buffer solution for application.

200. Use in accordance with one of the Claims 41 to 79, whereby the dsRNA I/II is administered orally or by intravenous, intratumoral, or intraperitoneal injection or infusion, or by inhalation.

201. Medicament for inhibiting the expression of a target gene in a cell containing a double-stranded ribonucleic acid (dsRNA I) in a dosage sufficient to inhibit the expression of the target gene.

whereby dsRNA I exhibits a double-stranded structure consisting of a maximum of 49 successive nucleotide pairs,

and whereby one strand (as1) or at least one segment of the strand (as1) of the double-stranded structure is complementary to the target gene,

and whereby at least one end (E1, E2) of the dsRNA I exhibits an overhang consisting of 1 to 4 nucleotides.

202. Medicament in accordance with Claim 81, whereby dsRNA I exhibits the overhang at the 3'-end of one strand (as1) and/or at the 3'-end of the other strand (ss1).

203. Medicament in accordance with Claim 81 or 82, whereby the dsRNA I has a smooth configuration at one end (E1, E2).

204. Medicament in accordance with Claim 83, whereby the smooth end (E1, E2) contains the 5'-end of the first strand (as1).

205. Medicament in accordance with Claims 81 to 84, whereby the overhang consists of 1 to 4 nucleotides, preferably of 1 or 2 nucleotides.

206. Medicament in accordance with one of the Claims 81 to 85, whereby at least one further double-stranded ribonucleic acid (dsRNA II) having a configuration according to the dsRNA I as defined in Claims 81 to 85, and whereby the one strand (as1) of dsRNA I is complementary to a first region

(B1) of the target gene, and whereby another strand (as2) or at least one segment of the other strand (as2) of dsRNA II is complementary to a second region (B2) of the target gene.

207. Medicament in accordance with one of the Claims 81 to 86, whereby the dsRNA I and/or dsRNA II exhibits a length of fewer than 25, preferably in 19 to 23, successive nucleotide pairs.

208. Medicament in accordance with one of the Claims 81 to 87, whereby the first (B1) and the second region (B2) overlap segmentally or adjoin each other.

209. Medicament in accordance with one of the Claims 81 to 88, whereby the target gene exhibits one of the sequences SQ001 to SQ140.

210. Medicament in accordance with one of the Claims 81 to 89, whereby the target gene is selected from the following group: oncogene, cytokine gene, Id protein gene, prion gene, genes from angiogenesis-inducing molecules, from adhesion molecules, and from cell-surface receptors; genes from proteins that are involved in metastatic and/or invasive processes; genes from proteinases as well as molecules that regulate apoptosis and the cell cycle.

211. Medicament in accordance with one of the Claims 81 to 90, whereby the target gene is the MRD1 gene.

212. Medicament in accordance with one of the Claims 81 to 91, whereby one of the sequences SQ141-173 or a dsRNA construct being combined of two antisense- (as1/2) and sense sequences (ss1/2) belonging together and belonging to sequences SQ141-173 are used as the dsRNA I/II.

213. Medicament in accordance with one of the Claims 81 to 92, whereby expression is inhibited according to the principle of RNA interference.

214. Medicament in accordance with one of the Claims 81 to 93, whereby the target gene is expressed in pathogenic organisms, most advantageously in plasmodia.

215. Medicament in accordance with one of the Claims 81 to 94, whereby the target gene is a component of a virus or viroid.

216. Medicament in accordance with Claim 95, whereby the virus is a human pathogenic virus or viroid.

217. Medicament in accordance with Claim 95, whereby the virus or viroid is a virus or viroid that is pathogenic in animals or plants.

218. Medicament in accordance with one of the Claims 81 to 97, whereby unpaired nucleotides are substituted with nucleoside thiophosphates.

219. Medicament in accordance with one of the Claims 81 to 98, whereby at least one end (E1, E2) of dsRNA I/II is modified in order to counter decomposition in the cell or dissociation in the individual strand.

220. Medicament in accordance with one of the Claims 81 to 99, whereby the cohesion of the double-stranded structure effected by the complementary nucleotide pairs is increased by at least one chemical bond.

221. Medicament in accordance with one of the Claims 81 to 100, whereby the chemical link is achieved either by a covalent or ionic bond, a hydrogen bond, hydrophobic interaction, preferably by means of van der Waals or stacking interactions, or by means of metal-ion coordination.

222. 102. Medicament in accordance with one of the Claims 81 to 101, whereby the chemical link is formed in the vicinity of one end (E1, E2).

223. Medicament in accordance with one of the Claims 81 to 102, whereby the chemical link is created by one or several linkage groups, whereby the linkage groups are preferably poly-(oxyphosphinico-oxy-1,3-propandiol) and/or oligoethyleneglycol chains.

224. Medicament in accordance with one of the Claims 81 to 103, whereby the chemical link is formed by using branched nucleotide analogs instead of nucleotides.

225. Medicament in accordance with one of the Claims 81 to 104, whereby the chemical link is formed by purine analogs.

226. Medicament in accordance with one of the Claims 81 to 105, whereby the chemical link is formed by azabenzene units.

227. Medicament in accordance with one of the Claims 81 to 106, whereby at least one of the following groups is used in creating the chemical link: methylene blue; bifunctional groups, preferably bis-(2-chlorethyl)-amine; N-acetyl-N'-(p-glyoxyl-benzoyl)-cystamine; 4-thiouracil; psoralen.

228. Medicament in accordance with one of the Claims 81 to 107, whereby the chemical link is formed by thiophosphoryl groups

that are attached in the vicinity of the ends (E1, E2) of the double-stranded region.

229. Medicament in accordance with one of the Claims 81 to 108, whereby the chemical link is formed by triple helix bonds that are present in the vicinity of the ends (E1, E2).

230. Medicament in accordance with one of the Claims 81 to 109, whereby the dsRNA I/II is enclosed in micellar structures, most advantageously in liposomes.

231. Medicament in accordance with one of the Claims 81 to 110, whereby the dsRNA I/II is bound to, associated with, or enclosed by at least one viral case protein that stems from a virus, is derived from it, or is synthetically produced.

232. Medicament in accordance with one of the Claims 81 to 111, whereby the coat protein is derived from polyomavirus.

233. Medicament in accordance with one of the Claims 81 to 112, whereby the coat protein contains Virus Protein 1 (VP1) and/or Virus Protein 2 (VP2) of the polyomavirus.

234. Medicament in accordance with one of the Claims 81 to 113, whereby at the formation of a capsid or capsid-like structure, the one side is turned toward the inside of the capsid or capsid-like structure.

235. Medicament in accordance with one of the Claims 81 to 114, whereby the one strand (as1, as2) of dsRNA I/II is complementary to the primary or processed RNA transcript of the target gene.

236. Medicament in accordance with one of the Claims 81 to 115, whereby the cell is a vertebrate cell or a human cell.

237. Medicament in accordance with one of the Claims 81 to 116, whereby the first (B1) and the second region (B2) are separated from each other.

238. Medicament in accordance with one of the Claims 81 to 117, whereby the dsRNA is administered at a maximum amount of 5 mg per dose.

239. Medicament in accordance with one of the Claims 81 to 118, whereby the dsRNA is mixed in a buffer solution for application.

240. Medicament in accordance with one of the Claims 81 to 119, whereby the dsRNA is administered orally or by intravenous, intratumoral, or intraperitoneal injection or infusion, or by inhalation.

Method for inhibiting the Expression of a Target Gene

The invention concerns a method, a use, and a medicament for inhibiting expression of a target gene.

Methods to inhibit the expression of medically or biotechnologically interesting genes using a double-stranded ribonucleic acid (dsRNA) are known from WO 99/32619 and WO 00/44895. Although the known methods are highly effective, there is nonetheless a need to further enhance their efficiency.

The object of the present invention is to remove the shortcomings in accordance with the state-of-the-art. In particular, a method, a use, and a medicament are to be disclosed, by which even more efficient inhibition of the expression of a target gene is achievable.

This object is solved by the features of Claims 1, 41, and 81. Advantageous embodiments result from features of Claims 2 to 40, 42 to 80, and 82 to 120.

Surprisingly, with the features claimed in this invention, a drastic enhancement is achieved in the effectiveness of inhibition of the expression of a target gene in vitro and in vivo. As a result of the particular formation of the dsRNA ends, both their efficiency in mediating the inhibitory action on the expression of a target gene as well as their stability can be affected in a targeted way. Active concentration in the cells is enhanced as a result of this enhanced stability.

In terms of the invention, "target gene" is understood to mean the DNA strand of a double-stranded DNA in the cell, which is complementary to a DNA strand, including all transcribed regions, that serves as a matrix for transcription. In other

words, the "target gene" is generally the sense strand. One strand, or antisense strand (as1) can be complementary to an RNA transcript or its processing products, e.g., an mRNA, formed during expression of a target gene. The term "introduced into" is understood to mean uptake in the cell. Uptake may occur by means of the cell itself. However, it may also be mediated by auxiliary agents or devices. "Overhang" is understood to mean a single-stranded projection located at an end, which does not exhibit Watson-Crick paired nucleotides. "Double-stranded structure" is understood to mean a structure in which the nucleotides of the individual strands are generally paired in accordance with Watson & Crick. In terms of the present invention, a double-stranded structure may also exhibit individual mismatches.

In a particularly advantageous embodiment, dsRNA I exhibits the overhang at the 3'-end of the strand or antisense strand as1 and/or at the 3'-end of the other strand or antisense strand ss1. dsRNA I may also be smooth at one end. In this case, the smooth end is advantageously located on the side of dsRNA I that (exhibits)[1] the 5'-end of a strand (antisense strand; as1). In this embodiment, dsRNA I exhibits very good effectiveness as well as great stability in the living organism. Total in vivo effectiveness is outstanding. The overhang consists advantageously of 1 to 4 nucleotides, preferably of 1 or 2 nucleotides.

In accordance with a further embodiment, the effectiveness of the method can be further enhanced when at least one further dsRNA II corresponding to the dsRNA I in the invention is introduced into the cell, whereby one strand, or at least a segment of one strand of the double-stranded structure of dsRNA

[1] the word "exhibits" is missing.

I is complementary to a first region of the sense strand of the target gene, and whereby another strand, or at least a segment of the other strand of the double-stranded structure of the dsRNA II is complementary to a second region of the sense strand of the target gene. Inhibition of expression of the target gene is markedly enhanced in this case. The first and second region can overlap segmentally, be adjacent to each other, or be separated.

It has further been shown to be advantageous when the dsRNA I and/or the further dsRNA II is fewer than 25 successive nucleotide pairs in length. A length of between 19 and 23 nucleotide pairs has been shown to be particularly effective. Efficiency can be further enhanced when single-stranded overhangs containing 1 to 4 nucleotides are present in the double strands preferably formed by 19 to 23 nucleotide pairs.

The target gene can, in accordance with a further embodiment, exhibit one of the sequences SQ001 to SQ140 shown in the appended sequence protocol. It may be selected from the following group: an oncogene; cytokinin gene; Id protein gene; prion gene; gene that expresses molecules that induce angiogenesis, adhesion molecules, and cell surface receptors; genes of proteins that are involved in metastasizing and/or invasive processes; genes of proteinases as well as of molecules that regulate apoptosis and the cell cycle; genes that express the EGF receptor. In particular, the target gene can be a MDR1 gene. It may be used in this connection a dsRNA I/II consisting of one of the sequences SQ141-173 or a combination of one of the antisense (as) and sense sequences (ss) that belong together.

In accordance with another advantageous embodiment, expression is inhibited according to the principle of RNA interference.

The target gene is advantageously expressed in pathogenic organisms, preferably in plasmodia. It can be a component of a virus or viroid, particularly a virus or viroid that is pathogenic in humans. The virus or viroid can also be one that is pathogenic in animals or plants.

In another embodiment, it is provided that the unpaired nucleotides are substituted by nucleoside thiophosphates.

At least one end of the dsRNA I/II may be modified to counteract decomposition in the cell or dissociation in the individual strands. Advantageously, the cohesion of the double-stranded structure that results from the complementary nucleotide pairs is enhanced by at least one chemical bond. The chemical bond may be achieved either by a covalent or ionic bond, a hydrogen bond, hydrophobic interaction, preferably by means of van der Waals or stacking interactions, or by means of metal-ion coordination. In addition, it has also been shown to be advantageous and stability-enhancing if the chemical bond occurs in the vicinity of one end. Other advantageous embodiments with regard to chemical bonding can be found in the features in Claims 24 to 30, and no further explanation is required.

dsRNA I/II may be particularly easily introduced into the cell when it is enclosed in micellar structures, preferably in liposomes. For the transport of dsRNA I/II into the cell, it has been found to be advantageous that they be bound, associated, or enclosed by at least one viral coat protein that stems directly from a virus, is derived from it, or is synthetically produced. The coat protein may be derived from a polyoma virus. In particular, the coat protein may contain Virus Protein 1 and/or Virus Protein 2 of the polyoma virus. In accordance with a further embodiment, it is provided that during formation of a capsid or capsid-like structure from coat protein, one side is

turned to the interior of in the capsid or capsid-like structure. Furthermore, it is advantageous that one strand of the dsRNA I/II (as1/2) is complementary to the primary or processed RNA transcript of the target gene. The cell may be either a vertebrate cell or a human cell.

Furthermore, it has been demonstrated that dsRNA I/II may be administered to mammals, preferably human beings, even at a maximum dose of 5 mg/kg body weight per day. Even at this low dosage effectiveness is outstanding.

Surprisingly, it has been shown that dsRNA I/II may be mixed in a buffer solution and then administered orally or by injection or infusion, either intravenously, intratumorally, intraperitoneally, or inhalationally.

Furthermore, the invention provides the use of a double-stranded ribonucleic acid (dsRNA I) to inhibit expression of a target gene in the cell, whereby dsRNA I exhibits a double-stranded structure consisting of a maximum of 49 successive nucleotide pairs, and whereby one strand (antisense strand, as1) or at least one segment of the strand of the double-stranded structure is complementary to the sense strand of the target gene, and whereby dsRNA I exhibits an overhang at one end consisting of 1 to 4 nucleotides.

In accordance with another measure of the invention, a medicament containing one double-stranded ribonucleic acid (dsRNA I) in a quantity sufficient to inhibit expression of the target gene in a cell is provided, whereby dsRNA I exhibits a double-stranded structure consisting of a maximum of 49 successive nucleotide pairs, and whereby one strand (as1) or at least one segment of one strand (as1) of the double-stranded structure is complementary to the sense strand of target gene,

and whereby the dsRNA I exhibits at least one overhang at one end consisting of 1 to 4 nucleotides.

Refer to the previous discussion for other advantageous embodiments of dsRNA I/II.

The invention will be explained on the basis of drawings and examples as follows. These show:

Fig. 1a, b diagram of a first and second double-stranded RNA and

Fig. 2 diagram of a target gene,

Fig. 3 relative YFP fluorescence after application of various dsRNAs in NIH/3T3 cells (first experiment),

Fig. 4 relative YFP fluorescence after application of various dsRNAs in NIH/3T3 cells (second experiment),

Fig. 5 relative YFP fluorescence after application of various dsRNAs in NIH/3T3 cells (third experiment),

Fig. 6 relative YFP fluorescence after application of various dsRNAs in NIH/3T3 cells (fourth experiment),

Fig. 7 relative YFP fluorescence after application of various dsRNAs in Hela-S3 cells (fifth experiment),

Fig. 8 fluorescence microscopic imaging of NIH/3T3 cells after transfection with pcDNA-YFP or after cotransfection with pcDNA-YFP and various dsRNAs,

Fig. 9 fluorescence microscopic imaging of HeLa-S3 cells after transfection with pcDNA-YFP or after cotransfection with pcDNA-YFP and various dsRNAs,

Fig. 10 gel electrophoretic separation of S1 after incubation in mouse serum,

Fig. 11 gel electrophoretic separation of S1 after incubation in human serum,

Fig. 12 gel electrophoretic separation of S7 after incubation in mouse serum,

Fig. 13 gel electrophoretic separation of S7 after incubation in human serum,

Fig. 14 gel electrophoretic separation of K3 after incubation in mouse serum,

Fig. 15 gel electrophoretic separation of PKC1/2 after incubation in mouse serum,

Fig. 16 gel electrophoretic separation of S1A/S4B after incubation in human serum,

Fig. 17 gel electrophoretic separation of K2 after incubation in human serum, and

Fig. 18 GFP-specific immunoperoxidase staining of kidney paraffin sections from transgenic GFP mice,

Fig. 19 GFP-specific immunoperoxidase staining of heart paraffin sections from transgenic GFP mice,

Fig. 20 GFP-specific immunoperoxidase staining of pancreas paraffin sections from transgenic GFP mice,

Fig. 21 Western blot analysis of GFP expression in plasma,

Fig. 22 Western blot analysis of GFP expression in kidney,

Fig. 23 Western blot analysis of GFP expression in heart,

Fig. 24 Western blot analysis of EGFR expression in U-87 MG glioblastoma cells,

Fig. 25a Northern blot analysis of the MDR1 mRNA level in colon carcinoma cell line LS174T, whereby the cells were harvested after 74 hours,

Fig. 25b quantification of the bands in Figure 25a, whereby the averages are represented by two values,

Fig. 26a Northern blot analysis of the MDR1 mRNA level in colon carcinoma cell line LS174T, whereby the cells were harvested after 48 hours,

Fig. 26b quantification of the bands in Figure 26a, whereby the averages of two values are represented,

Fig. 27 comparison of a transmitted light- and fluorescence microscopic imaging of a transfection with 175 nM dsRNA (Sequence R1 in Table 4).

The double-stranded ribonucleic acids dsRNA I and dsRNA II depicted schematically in Figures 1a and 1b each exhibit a first end (E1) and a second end (E2). The first and the second ribonucleic acids dsRNA I/dsRNA II exhibit single-stranded

segments at both ends (E1, E2), being formed of approximately 1 to 4 unpaired nucleotides. Two possible variants are shown (Variants 1 and 2), whereby Variant 2 exhibits a smooth end (E2). The smooth end may, however, be situated at the other end (E1) in other variants.

Figure 2 shows schematically a target gene located on a DNA. The target gene has been made visible by means of a black line. It exhibits a first region (B1) and a second region (B2).

In each case, one strand of the first dsRNA I (as1) or of the second dsRNA II (as2) is complementary to the corresponding region B1 or B2 in the target gene, respectively.

Expression of the target gene is inhibited particularly effectively when dsRNA I/dsRNA II exhibits single-stranded segments at their ends (E1, E2). The single-stranded segments may be located both on strand as1 or as2, or on anti-strand (ss1 or ss2), or on strand as1, as2, and on the anti-strand.

Regions B1 and B2 may be separated from each other as shown in Figure 2. However, they may also adjoin or overlap.

I. Inhibition of the expression of the YFP gene in fibroblasts:

Double-stranded RNAs were derived from sequences of Yellow Fluorescent Proteins (YFP), a variant of GFP (Green Fluorescent Protein) from the *Aequoria victoria* alga, and microinjected into fibroblasts together with a YFP-coding plasmid. Subsequently, the decrease in fluorescence compared to cells without dsRNA was analyzed.

Experiment protocol:

Single RNA strands and their complementary single strands were synthesized from sequence protocols SQ148, SQ149 and SQ159,

using an RNA synthesizer (Expedite 8909, Applied Biosystems, Weiterstadt, Germany) and conventional chemical processes. These were subsequently purified using HPLC. Hybridization of the individual strands into double strands was done by heating up the stochiometric mixture of the single strands in 10 mM of sodium phosphate buffer, pH 6.8, and 100 mM NaCl to 90°C, and then allowing it to cool off slowly for 6 hours to room temperature. The dsRNA that was obtained in this way was microinjected into the test cells.

The test system used for this cell culture experiment was the murine fibroblast cell line NIH/3T3, ECACC No. 93061524 (European Collection of Animal Cell Culture). The pcDNA-YFP plasmid, which contains an 800bp Bam HI/Eco RI-YFP fragment in the corresponding restriction site of the pcDNA3 vector, was used for the microinjections. Expression of YFP under the influence of simultaneously transfused sequence-homologous dsRNA was studied. Analysis of green fluorescence under the fluorescence microscope was done 3 hours after injection at the earliest.

Preparation of the cell cultures:

The cells were incubated in DMEM with 4.5 g/l glucose and 10% fetal calf serum (FCS), 2 mM L-glutamine, and penicillin/streptomycin (100 IU/100 µg/ml, Biochrom) in an incubator in an atmosphere containing 5% CO_2 at 37°C. The cells were passaged every 3 days in order to maintain them in an exponential growth state. One day before transfection, the cells were trypsinized (10x trypsin/TEDTA, Biochrom) and placed in coated petri dishes (CORNING Cell Culture Dish, 35 mm, Corning Inc., Corning NY) at a cell density of 0.3×10^5. The petri dishes were incubated for at least 30 minutes at 37°C with 0.2% gelatin (Biochrom), washed once with PBS, and used immediately to

culture the cells. In order to find the individual cells again, CELLocate coverslips were used (square sized 55µm, Eppendorf).

Microinjection:

The petri dishes were taken out of the incubator approximately 10 minutes prior to microinjection. Approximately 50 cells per dish and per incubate were microinjected (FemtoJet, Micromanipulator 5171, Eppendorf). Glass capillaries (FemtoTip, Eppendorf) with an internal tip diameter of 0.5 µm were used. Injection time was 0.8 seconds at a pressure of 30 hPA. Microinjection took place under an Olympus IX50 microscope equipped for fluorescence. The injection buffer used consisted of 14mM NaCl, 3 mM KCl, and 10 mM KH_2PO_4, pH 7.0, which contained 0.01 µg/µl pcDNA-YFP. An injection solution of 0.08% (w/v) Texas red coupled with dextran 70000 (Molecular Probes, Leiden, Netherlands) was added to test for successful microinjection. In order to analyze the inhibition of YFP expression with specific dsRNA, dsRNAs were added to the injection solution: Assay 1: 0.01 µM dsRNA (sequence protocol SQ148/149); Assay 2: 0.01 µM dsRNA (sequence protocol SQ148/159); Assay 3: without RNA. After microinjection, the cells were incubated for at least another 3 hours in an incubator. Intracellular YFP fluorescence was then analyzed under the microscope: the cells that fluoresced both red and green simultaneously: microinjection was successful, no inhibition of YFP expression as a result of dsRNA was observed, or there were control cells into which no dsRNA was injected; only red fluorescent cells: microinjection was successful, dsRNA inhibited YFP expression.

Results:

At a dsRNA concentration of 0.1 µM, the use of dsRNA with single-stranded regions with two-nucleotide overhangs each at both 3'-ends (sequence protocol SQ148/159) markedly enhanced inhibition of the expression of the YFP gene in fibroblasts in

comparison to dsRNA without end having single overhanging strands (Table 1).

The use of short dsRNA molecules, containing 19-25-base pairs with overhangs consisting of a few, preferably 1 to 3, non-base-paired single-stranded nucleotides thus makes possible a comparatively more powerful inhibition of gene expression in mammalian cells than does the use of dsRNAs with the same number of base pairs without the corresponding single-stranded overhangs at the same RNA concentrations.

Assay	**Name**	**Sequence protocol No.**	**0.1 µM**
1	**S1A/** **S1B**	SQ148 SQ149	+
2	**S1A/** **S4B**	SQ148 (overhanging ends) SQ159	+++
3		Without RNA	-

Table 1: The symbols give the relative proportion of non- or weakly-fluorescent cells (+++ > 90%; ++ 60-90%-+ 30-60%; - < 10%).

II. Inhibition by dsRNA of gene expression of a target gene in cultured HELA-S3 cells and mouse fibroblasts:

The effectiveness of the inhibition of YFP expression after transient transfection of a YFP-coding plasmid on the basis of RNA interference with dsRNA may be modulated by manipulating the 3'-ends and the length of the base-paired region.

Example:

In order to determine the effectiveness of dsRNA in the specific inhibition of gene expression, transient transfected NIH/3T3

cells (fibroblasts from NIH Swiss mouse embryo, ECCAC [European collection of animal cell culture] No. 93061524) and HELA-S3 (human cervical cancer cells, DSMZ [German collection of microorganisms and cell cultures] No. ACC 161) were used. The pcDNA-YFP plasmid, containing an 800-bp Bam HI/Eco RI-YFP fragment in the corresponding cleaving sites of the vector pcDNA 3, was used for transfection. Double-stranded RNAs (dsRNAs) derived from the sequence of the yellow fluorescent protein (YFP) were produced and transiently transfected into the fibroblasts along with the pcDNA-YFP plasmid (the antisense strands of the specific dsRNAs used are complementary to the corresponding segments of the gene sequences of both YFP and GFP). The reduction in fluorescence was quantified after 48 hours. Cells that were either transfected only with pcDNA-YFP or with pcDNA-YFP and a control dsRNA (not derived from the YFP sequence) were used as controls.

Test protocol:

dsRNA synthesis:

The individual RNA strands seen in the sequence protocols as well as their complementary single strands were synthesized using an RNA synthesizer (Expedite 8909, Applied Biosystems, Weiterstadt, Germany), as well as by conventional chemical means. Purification of the raw synthesis products was then done with the help of the HPLC. The NucleoPac PA-100, 9 x 250 column (Dionex) was used with 20 mM tris, 10 mM $NaClO_4$, pH 6.8, 10% acetonitrile were used as the low salt buffer, and 20 mM tris, 400 mM $NaClO_4$, pH 6.8, 10% acetonitrile were used as the high salt buffer. Flow was 3 ml per minute. Hybridization of the single strands into a double-stranded was done by heating the stochiometric mixture of the single strands in 10 mM sodium phosphate buffer, pH 6.8, and 100 mM NaCl to 80-90°C and then allowing it to cool slowly over 6 hours to room temperature.

Seeding the cells:

All cell culturing was conducted under sterile conditions at an appropriate workstation (HS18/ Hera Safe, Kendro, Heraeus). Culturing of the NIH/3T3 cells and the HELA-S3 was done in the incubator (CO_2-incubator T20, Hera Cell, Kendro, Heraeus) at 37°C, 5% CO_2, and saturated atmospheric humidity in DMEM (Dulbecco's modified eagle medium, Biochrom) for the mouse fibroblasts, and in Ham's F12 for the HELA cells, with 10% FCS (fetal calf serum, Biochrom), 2 mM L-glutamine (Biochrom), and penicillin/streptomycin (100 IU/100µg/ml, Biochrom). In order to maintain the cells in an exponential growth state, the cells were passaged every 3 days. Twenty-four hours before transfection, the cells were trypsinized (10x trypsin/EDTA, Biochrom, Germany) and placed in a 96-well plate (Multiwell Schalen 96-well, flat-bottom, Schubert & Weiss Laboratories, GmbH) at a cell density of 1.0×10^4 cells/depression and cultured in 150 µl growth medium.

Implementation of transient transfection:

Transfection was done using Lipofectamine Plus™ reagent (Life Technologies) in accordance with manufacturer directions. 0.15 µg pcDNA-YFP plasmid was placed in each well. The entire transfection volume was 60 µl. In each case, 3 samples were started. First, the plasmid DNA was complexed together with the dsRNA. The plasmid DNA and dsRNA were diluted in serum-free medium, and 1 µl PLUS reagent was used per 0.1 µg of plasmid DNA (in a volume of 10 µl). This was then incubated at room temperature after mixing for 15 minutes. During incubation 0,5 µl lipofectamine was diluted in 10µl serum-free medium per 0,1 µg plasmsid-DNA, well mixed, added to the plasmid/dsRNA/PLUS-mixture and again incubated for 15 minutes. The medium was changed during incubation. The cells were washed once with 200

µl serum-free medium, and thereafter incubated with 40 µl serum-free medium in the incubator until the addition of DNA/dsRNA/PLUS/Lipofectamine. After the addition of 20 µl DNA/dsRNA/PLUS/Lipofectamine per well, the cells were incubated in an incubator for 2.5 hrs. After incubation, the cells were washed once with 200 µl growth medium and incubated in the incubator for 24 hours in 200 µl growth medium until fluorescence detection was done.

Fluorescence detection:

24 hours after the last medium change, cell fluorescence was photographed using a fluorescence microscope (IX50-S8F2,U-ULS100Hg fluorescence unit, Brenner U-RFL-T200, Olympus) with a USH I02D mercury lamp (Ushio Inc., Tokyo, Japan), fitted with a WIB fluorescence cube and a digital CCD camera (Orca IIIm, Hamamatsu), and a C4742-95 preview monitor. Analysis of the fluorescence images was done using Analysis Software 3.1 (Soft Imaging System GmbH, Germany. In order to relate YFP fluorescence to cell density, cell nucleus staining was done (Hoechst staining). For this the cells were fixed, first in 100 µl methylcarnoy (75% methanol, 25% glacial acetic acid) for 5 minutes, and then again for 10 minutes in methylcarnoy. After air drying, the fixed cells were incubated in the dark for 30 minutes with 100 µl Hoechst stain per well (75 ng/ml). After washing twice with PBS (Dulbecco PBS w/o Ca^{2+}, Mg^{2+}, Biochrom), the cells that had been Hoechst stained were photographed under the fluorescence microscope (Olympus, WU fluorescence cube for Hoechst).

The results regading inhibition of YFP expression in cultivated cells by dsRNA are summarized in Figures 3 to 9: The effects of YFP-specific dsRNAs and of control dsRNAs on YFP expression in NIH/3T3 mouse fibroblasts after transient transfection are summarized in Figures 3, 4, 5, and 6. The experiments were

carried out as described in the test protocol. The concentration of dsRNA relates to the concentration in the medium during the transfection reaction. The dsRNA designations may be seen in Table 2. It shows the relative fluorescence per photographic image in terms of surface percentage. Three different photographic images were analyzed per well. The average values are obtained from the three images.

Specific inhibition of YFP-gene expression by dsRNAs in HELA-S3 cells is shown in Figures 7 and 9. Figure 7 shows the inhibiting action of variously configured dsRNA constructs (Table 2) in various concentrations on expression of YFP in HeLa cells. Figure 8 shows representative fluorescence microscopic images of NIH/3T3 mouse fibroblasts transiently transfected with YFP, without dsRNA and with specific anti-YFP-directed dsRNAs (100x enlargement).

8A: YFP control
8B: S1, 10 nM
8C: S4, 10 nM
8D: S7, 10 nM
8E: S7/S11, 1 nM
8F: S7/S12, 1 nM

Figure 9 shows representative fluorescence microscopic images of HELA-3S cells transiently transfected with YFP, without dsRNA and with specific anti-YFP-directed dsRNAs (100x enlargement).
9A: K2 control, 10 nM
9B: S1, 10 nM
9C: S4, 10 nM
9D: S7, 10 nM
9E: S7/11, 1 nM
9F: S7/12, 1 nM
9G: S1A/S4B, 10 nM

9H: YFP control

Results:

Figure 3 shows that YFP expression after transient cotransfection of mouse fibroblasts with the YFP plasmid and specific anti-YFP-sequence-directed dsRNAs can be particularly effectively inhibited when the 3'-ends of the 22- and 19-base-pair-containing regions of the dsRNAs exhibit single-stranded segments of 2 nucleotides (nt). Whereas the S1 dsRNA with smooth 3'-ends exhibits no inhibitory effects on YFP expression at a concentration of 1 nM (relating to the concentration in the cell culture medium during transfection), the S7 dsRNA (19 nucleotide pairs) and the S4 (22 nucleotide pairs), each with 2nt overhangs at both 3'-ends, inhibited YFP expression by 50% and 70%, respectively, in comparison to the corresponding control dsRNAs (K3 and K2). At a concentration of 10 nM, the dsRNA with the smooth ends designated S1 inhibits YFP expression by ~65%, whereas the S4 dsRNA inhibits YFP expression by ~93% (Figure 4). The inhibitory effects of the dsRNAs designated as S4 and S7 are concentration-dependent (Figure 3 and 4; see also Figure 7).

Figure 4 shows that the single-stranded configuration at both 3'-ends (of the sense and antisense strand) is not necessary for efficient suppression of YFP gene expression. To achieve effective inhibition of YFP expression, only the 2nt overhang at the 3'-end of the antisense strand is necessary. Thus, for both S4 dsRNAs (with 2nt overhangs at both 3'-ends) and S1A/S4B (with one 2nt overhang at the 3'-end of the antisense strand) inhibition of YFP expression at a concentration of 1 nM is ~70%. However, if on the other hand the 2nt overhang is located at the 3'-end of the sense strand (and the 3'-end of the antisense strand does not have a single-stranded region), inhibition of

YFP gene expression is 50%. Analogously, inhibition at higher concentrations is considerably better when at least the 3'-end of the antisense strand has a 2nt overhang.

A more marked inhibition of YFP expression is achieved when the base-paired region has 21 nucleotide pairs instead of 22 (S1 and S4), 20 (S13 or S13/14, or 19 (S7) (Figures 5, 6, and 7). Thus, at a concentration of 5 nM, inhibition of YFP expression by S1 (22 base pairings with smooth ends) is ~40%, while inhibition by S7/S12 (21 base pairings with smooth ends), also at 5 nM, is ~92%. If the dsRNA with 21 base pairings exhibits another 2nt overhang at the antisense strand 3'-end (S7/S11), inhibition is ~97% (compared with ~73% inhibition by S4 and ~70% inhibition by S7).

III. Analysis of serum stability of double-stranded RNA (dsRNA):

The object is to take the effectiveness of the inhibition on the gene expression of target genes mediated by dsRNAs found in cell cultures and enhance it for use in vivo. This is achieved by improving the stability of dsRNA in serum, and by increasing the retention time of the molecule in the blood circulation, or by increasing the effective concentration of the functional molecule that results from the foregoing.

Example:

Serum stability of GFP-expression-inhibiting dsRNAs was tested ex vivo in murine and human serum.

Test protocol:

Incubation of human and murine serum with corresponding dsRNA was done at 37°C. In each case, 85µl serum was incubated with 15

µl 100µM dsRNA. After certain incubation spans (30 minutes, 1 hour, 2 hours, 4 hours, 8 hours, 12 hours, 24 hours) the samples were frozen at -80°C. DsRNA without serum (+85 µl ddH_2O) and dsRNA with serum at Time 0 were used as controls.

In order to isolate dsRNA from the incubate, which was done on ice, 400 µl 0.1% SDS was added to each incubate, and these then underwent phenol extraction: 500 µl phenol:chloroform:isoamyl alcohol (IAA, 25:24:1, Roti phenol, Roth, Karlsruhe) were added to each incubate, and then vortexed at the highest setting for 30 seconds (Vortex Genie-2, Scientific Industries). After incubation for 10 minutes on ice, phase separation was carried out by centrifugation at 12,000 xg at 4°C for 10 minutes (Sigma 3K30, Rotor 12131-H). The top aqueous phase (approximately 200 µl) was collected and then underwent digestion: first with DNase I and then with Proteinase K: 20 µl 10x DNase buffer (100 mM tris, pH 7.5, 25 mM MgCl2, 1 mM CaCl2) and 10 U DNase I (D 7291, Sigma-Aldrich) were added incubated for 30 minutes at 37°C, then 6 U DNase I were again added, incubated for another 20 minutes at 37°C. Then 5µl Proteinase K (20 mg/ml, 04-1075, Peqlab, Germany) was added and incubated for 30 minutes at 37°C. Phenol extraction was then carried out. To this was added 500 µl phenol:chloroform:IAA (25:24:1), vortexed for 30 seconds at the highest setting, and then centrifuged for 10 minutes at 12,000 xg and 4°C. The supernatant fluid was drawn off and replaced sequentially with 40 µl 3 M Na-Ac (sodium acetate), pH 5.2, and 1 ml 100% EtOH; this was well mixed and precipitated for at least one hour at -80°C. The precipitate was pelleted by centrifugation at 12,000 xg for 30 minutes at 4°C, washed with 70% EtOH, and again centrifuged (10 minutes, 12,000 xg at 4°C). The air-dried pellet was then mixed in 30 µl RNA gel application buffer (7 M urea, 1 x TBE [0.09 M tris borate, 0.002 M EDTA, 0.02% [w/v] bromophenol blue, 0.2% [w/v] xylencyanol) and stored at -20°C until gel application.

In order to characterize the dsRNA, analytic, denaturing polyacrylamide gel electrophoresis (analytic PAGE) was carried out. The urea gels were produced shortly before the run: 7M urea (21 g) was dissolved while stirring in 25 ml 40% aqueous acrylamide/bisacrylamide solution (Rotiphoresis gel, A515.1, Roth) and 5 ml 10 x TBE (108 g tris, 55 g boric acid, 3.9 g EDTA per liter distilled water) and diluted to 50 ml with of distilled water. Shortly before pouring, 50 µl TEMED (N,N,N',N'-tetramethyl ethylendiamine) and 500 µl 10% APS (ammonium peroxide sulfate) were added. After polymerization, the gel was placed in a vertical electrophoresis apparatus (Merck, Darmstadt), and a first fraction was carried out for 30 minutes at a constant amperage of 40 mA. 1 x TBE buffer was used as the running buffer. Before applying them to the gel, the RNA samples were heated for 5 minutes at 100°C, cooled on ice, and then centrifuged for 20 seconds on a table centrifuge (Eppendorf Minispin). 15 µl of each sample was applied to the gel. The test run lasted for approximately two hours at a constant amperage of 40 mA. After the run, the gel was stained with Stains All staining solution (20 ml Stains All solution [200 mg Stains All dissolved in 200 ml formaldehyde] with 200 ml of distilled water and 100 ml formamide), and the background stain was then removed by rinsing with distilled water for 45 minutes. The gels were photographed using the Image Master VDS photodocumentation system from Pharmacia. Figures 10 to 17 show the serum stability of dsRNA after incubation with human or murine serum, and subsequent electrophoretic separation in 20% 7M urea gel.

Figure 10: Incubation of S1 (0-22-0) in mouse serum

1. At Time 0 (without serum)
2. At Time 0
3. For 30 minutes
4. For 1 hour
5. For 2 hours

6. For 4 hours
7. For 12 hours
8. 2 µl 100 µM S1 without incubation

S1A) sense strand S1 (10 µl 20 µM S1A)
S1B) antisense strand S1 (10 µl 20 µM S1B)

Figure 11: Incubation of S1 (0-22-0) in human serum

1. 2 µl 100 µM S1 untreated (without incubation)
2. For 30 minutes
3. For 2 hours
4. For 4 hours
5. For 6 hours
6. For 8 hours
7. For 12 hours
8. For 24 hours

S1A) sense strand S1 (10 µl 20 µM S1A)
S1B) antisense strand S1 (10 µl 20 µM S1B)

Figure 12: Incubation of S7 (2-19-2) in mouse serum

1. At Time 0 (without serum)
2. For 30 minutes
3. For 4 hours
4. For 12 hours

Figure 13: Incubation of S7 (2-19-2) in human serum

1. Sense strand S7 (10 µl 20 µM S7A)
2. Antisense strand S7 (10 µl 20 µM S7B)
3. For 30 minutes
4. For 1 hour
5. For 2 hours
6. For 4 hours
7. For 6 hours
8. For 12 hours
9. For 24 hours
10. At Time 0 (without serum)

Figure 14: Incubation of K3 (2-19-2) in mouse serum

1. Sense strand K3 (10 µl 20 µM K3A)
2. Antisense strand K3 (10 µl 20 µM K3B)
3. At Time 0 (without serum)
4. At Time 0 (with serum)
5. For 30 minutes
6. For 1 hour
7. For 2 hours
8. For 4 hours
9. For 12 hours

Figure 15: Incubation of PKCl/2 (0-22-2) in mouse serum

1. For 30 minutes
2. For 1 hour
3. For 2 hours
4. For 4 hours
5. For 12 hours
6. 2 µl 100µM PKCl/2 (untreated)

Figure 16: Incubation of S1A/S4B (0-22-2) in human serum

1. At Time 0 (without serum)
2. For 24 hours
3. For 12 hours
4. For 8 hours
5. For 6 hours
6. For 4 hours
7. For 2 hours
8. For 30 minutes
9. Sense strand S1A (10 µl 20 µM S1A)
10. Antisense strand S4B (10 µl 20 µM S4B)

Figure 17: Incubation of K2 (2-22-2) in human serum

1. Sense strand K2 (10 µl 20 µM K2A)
2. Antisense strand K2 (10 µl 20 µM K2B)
3. At Time 0 (without serum)
4. For 30 minutes
5. For 2 hours
6. For 4 hours
7. For 6 hours
8. For 8 hours
9. For 12 hours
10. For 24 hours

Results:

DsRNAs without single-stranded regions at the 3'-ends are considerably more stable in both human and mouse serum than are dsRNAs with single-stranded 2nt overhangs at the 3'-ends (Figures 10 to 14 and 17). After 12 and 24 hours, respectively, of incubation of S1 in both murine and human serum, one band of the original size remains almost completely intact. By contrast, the stability of dsRNAs with 2nt overhangs at both 3'-ends decreases considerably in both human and murine serum. Even

after only 4 hours of incubation of S7 (Figures 12 and 13) or K3 (Figure 14), no band of the original size is still detectable.

In order to enhance the stability of dsRNA in serum, it is sufficient if the dsRNA possesses one smooth end. The original size of the band has hardly been broken down at all in mouse serum after 4 hours incubation (Figure 15, Track 4) when compared to S7 (complete decomposition after 4 hours; Figure 12, Track 3)

One optimal compromise with regard to the biological effectiveness of dsRNA may be the use of dsRNA with one smooth end and one single-stranded region of 2 nucleotides, whereby the single-stranded overhang is located at the 3'-end of the antisense strand.

The sequences used here are reproduced in the following Table 2 and in the sequence protocols SQ148-151 and 153-167.

Name	Sequence protocol No.	dsRNA-Sequence	
S1	SQ148 SQ149	(A) 5'- CCACAUGAAGCAGCACGACUUC -3' (B) 3'- GGUGUACUUCGUCGUGCUGAAG -5'	0-22-0
S7	SQ150 SQ151	(A) 5'- CCACAUGAAGCAGCACGACUU -3' (B) 3'- CUGGUGUACUUCGUCGUGCUG -5'	2-19-2
K1	SQ153 SQ154	(A) 5'- ACAGGAUGAGGAUCGUUUCGCA -3' (B) 3'- UGUCCUACUCCUAGCAAAGCGU -5'	0-22-0
K3	SQ155 SQ156	(A) 5'-GAUGAGGAUCGUUUCGCAUGA-3' (B) 3'-UCCUACUCCUAGCAAAGCGUA-5'	2-19-2
K2	SQ157	(A) 5'- ACAGGAUGAGGAUCGUUUCGCAUG -3'	

	SQ158	(B)	3´- UCUGUCCUACUCCUAGCAAAGCGU -5´	2-22-2
S1A/ S4B	SQ148	(A)	5´- CCACAUGAAGCAGCACGACUUC -3´	
	SQ159	(B)	3´- CUGGUGUACUUCGUCGUGCUGAAG -5´	0-22-2
PKC 1/2	SQ160	(A)	5´- CUUCUCCGCCUCACACCGCUGCAA -3´	
	SQ161	(B)	3´- GAAGAGGCGGAGUGUGGCGACG -5´	2-22-0
S7/S12	SQ150	(A)	5´- CCACAUGAAGCAGCACGACUU -3´	0-21-0
	SQ162	(B)	3´- GGUGUACUUCGUCGUGCUGAA -5´	
S7/S11	SQ150	(A)	5´- CCACAUGAAGCAGCACGACUU -3´	
	SQ163	(B)	3´- CUGGUGUACUUCGUCGUGCUGAA -5´	0-21-2
S13	SQ164	(A)	5´- CCACAUGAAGCAGCACGACU -3´	
	SQ165	(B)	3´- CUGGUGUACUUCGUCGUGCUGA -5´	0-20-2
S13/14	SQ164	(A)	5´- CCACAUGAAGCAGCACGACU -3´	
	SQ166	(B)	3´- GGUGUACUUCGUCGUGCUGA -5´	0-20-0
S4	SQ167	(A)	5´- CCACAUGAAGCAGCACGACUUCUU -3´	
	SQ159	(B)	3´- CUGGUGUACUUCGUCGUGCUGAAG -5´	2-22-2
K1A/ K2B	SQ153	(A)	5´- ACAGGAUGAGGAUCGUUUCGCA -3´	0-22-2
	SQ158	(B)	3´- UCUGUCCUACUCCUAGCAAAGCGU -5´	
K1B/ K2A	SQ154	(A)	5´- ACAGGAUGAGGAUCGUUUCGCAUG -3´	
	SQ157	(B)	3´- UGUCCUACUCCUAGCAAAGCGU -5´	2-22-0
S1B/ S4A	SQ149	(A)	5´- CCACAUGAAGCAGCACGACUUCUU -3´	
	SQ167	(B)	3´- GGUGUACUUCGUCGUGCUGAAG -5´	2-22-0

Table 2

IV. In vivo study:

Double-stranded RNA (dsRNA) that was derived from the GFP sequence and nonspecific dsRNA, respectively, was injected into

the caudal vein of "GFP lab mice" that express the green fluorescent protein (GFP) in all cells that are involved in protein biosynthesis. At the end of the experiment the animals were killed and tissue sections and plasma GFP expression were analyzed.

Test protocol:

dsRNA synthesis:

The individual RNA strands seen in the sequence protocols as well as their complementary individual strands were synthesized using an RNA synthesizer (Expedite 8909, Applied Biosystems, Weiterstadt, Germany), as well as by conventional chemical means. Purification of the raw synthesis products was then done with the help of the HPLC. The NucleoPac PA-100, 9 x 250 column (Dionex) was used: 20 mM tris, 10 mM $NaClO_4$, pH 6.8, 10% acetonitrile was used as the low salt buffer, and 20 mM tris, 400 mM $NaClO_4$, pH 6.8, 10% acetonitrile was used as the high salt buffer. Flow was 3 ml per minute. Hybridization of the individual strands into a double-stranded was done by heating the stochiometric mixture of the individual strands in 10 mM sodium phosphate buffer, pH 6.8, 100 mM NaCl to 80-90°C and then allowing it to cool slowly over 6 hours to room temperature.

Test-animal conditions and course of the experiment:

The transgenic laboratory mouse strain TgN(GFPU)5Nagy (Jackson Laboratory, Bar Harbor, ME) was used; this strain has been shown to express GFP (with a beta-actin promoter and a CMV intermediate early enhancer) in all previously tested cells, (Hadjantonakis AK et al., 1993, Mech Dev. 76:79-90; Hadjantonakis AK et al., 1998, Nature Genetics 19: 220-222). The GFP-transgenic mice may be readily differentiated from the corresponding wild type (WT) on the basis of fluorescence (using a hand-held UV lamp). The corresponding WT was always paired

with a heterozygote GFP type for purposes of breeding. The experiment was conducted in accordance with the German animal rights laws. The animals were kept in a controlled environment in groups of 3-5 animals in Type III Makrolon cages (Ehret, Emmendingen) at a constant temperature of 22°C and a day/night rhythm of 12 hours. Wood shavings of 8/15 granulated softwood (Altomin, Lage) were used. The animals received tap water and standard feed (Altormin 1324 pellets) ad libitum.

The heterozygote GFP animals that were used in the experiment were kept in cages in groups of 3 animals as described above. Injection of dsRNA solution was done intravenously (i.v.) in the caudal vein in 12-hour cycles (between 5:30 and 7:00 and between 17:30 and 19:00) over a 5-day period. Injection volume was 60 µl per 10 g of body weight, and the dosage was 2.5 mg dsRNA or 50 µg, respectively, per kg body weight. The groups were divided as follows:

Group A: PBS (phosphate buffered saline) 60 µl per 10 g body weight each,

Group B: 2.5 mg per kg body weight of a nonspecific control dsRNA (K1 control with smooth ends and a double-stranded region consisting of 22 nucleotide pairs),

Group C: 2.5 mg per kg body weight of another nonspecific control dsRNA (K3 control with 2nt overhangs at both 3'-ends and a double-stranded region consisting of 19 nucleotide pairs),

Group D: 2.5 mg per kg body weight dsRNA (specific anti-GFP directed, henceforth referred to as S1, with

smooth ends and a double-stranded region consisting of 22 nucleotide pairs),

Group E: 2.5 mg dsRNA per kg body weight (specific anti-GFP, henceforth referred to as S7, with 2nt overhangs at the 3'-ends of both strands and a double strand region consisting of 19 nucleotide pairs),

Group F: 50 µg S1 dsRNA per kg body weight (in other words 1/50 of the dosage in Group D).

After the last of a total of 10 injections, the animals were killed after 14-20 hours, and the organs and blood were removed as described.

Organ removal:

Immediately after the animals were killed by means of CO_2 inhalation, their blood and various organs were removed (thymus, along, heart, spleen, stomach, intestines, pancreas, brain, kidneys, and liver). The organs were quickly rinsed with cold, sterile PBS and sectioned using a sterile scalpel. One portion was fixed for 24 hours in methyl carnoys (MC, 60% methanol, 30% chloroform, 10% glacial acetic acid) for immunohistochemical staining; one portion was immediately flash-frozen in liquid nitrogen and stored at -80°C for making frozen sections and for protein isolation; and another, smaller portion, was frozen in RNAeasy Protect (Qiagen) at-80°C for RNA isolation. Immediately after removal, the blood was placed on the ice for 30 minutes, mixed, and centrifuged for 5 minutes at 2000 rpm (Mini spin, Eppendorf). The supernatant fluid (here referred to as plasma) was drawn off and stored at -80°C.

Processing the biopsies:

After the tissues had been fixed for 24 hours in MC, the tissue pieces were dehydrated in an ascending alcohol series at room temperature: 40 minutes each, 70% methanol, 80% methanol, 2 x 96% methanol and 3 x 100% isopropanol. After that, the tissue was warmed in an incubator in 100% isopropanol at 60°C, after which it was incubated for one hour in an isopropanol/paraffin mixture at 60°C and 3x for 2 hours in paraffin, and then bedded in paraffin. For the immunoperoxidase stains, the tissue sections 3 µm in thickness were prepared, using a rotation microtome (Leica), placed on glass slides (Superfrost, Vogel) and incubated for 30 minutes in an incubator at 60°C.

Immunoperoxidase staining for GFP:

The sections were deparaffinized 3 x 5 minutes in xylol, rehydrated in a descending alcohol series (3 x 3 min., 100% ethanol, 2 x 2 min. 95% ethanol), and then incubated in 3% H_2O_2/methanol to block endogenous peroxidases. All incubation steps in the following were carried out in a moist chamber. After washing with PBS 3 x 3 minutes, incubation was carried out with the first antibody (goat anti-GFP, sc-5384, Santa Cruz Biotechnology) 1:500 in 1% BSA/PBS overnight at 4°C. Incubation with the biotinylated secondary antibody (donkey anti-goat; Santa Cruz Biotechnology; dilution 1:2000) was then carried out for 30 minutes at room temperature, after which it was incubated with Avidin D peroxidase (dilution 1:2000, Vector Laboratories). After each antibody incubation, the sections were washed in PBS for 3 x 3 minutes, and the buffer residue and cell debris were removed from the sections. All antibodies were diluted in 1% bovine serum albumin (BSA)/PBS. Staining with 3,3'-diaminobenzadine (DAB) was done using a DAB substrate kit (Vector Laboratories) in accordance with manufacturer instructions. Gill's Hematoxylin III was used for the nucleic counter stain (Merck). After dehydration in an ascending alcohol series and 3 x 5 minutes xylol, the sections were covered with

Entellan (Merck). Microscopic analysis of the stains was done using an Olympus IX50 microscope fitted with a CCD camera (Hamamatsu).

Protein isolation from tissue pieces:

800 µl isolation buffer (50mM HEPES, pH 7.5; 150 mM NaCl; 1 mM EDTA; 2.5 mM EGTA; 10% glycerol; 0.1% Tween; 1 mM DDT; 10 mM β-glycerol phosphate; 1 mM NaF; 0.1mM Na_3VO_4 with a "Complete" protease inhibitor tablet manufactured by Roche) was added to each of the still-frozen tissue pieces, and then homogenized 2 x 30 seconds using an Ultraturrax (DIAX 900, 6G disperser, Heidolph), and cooled on ice between homogenization steps. After incubation on ice for 30 minutes, it was mixed and centrifuged for 20 minutes at 10,000 xg, at 4°C (3K30, Sigma). The supernatant fluid was then again incubated on ice for 10 minutes, mixed, and centrifuged for 20 minutes at 15,000 xg. Protein determination was then done on the supernatant fluid according to Bradford, 1976, modified according to Zor & Selinger, 1996, using the Roti-Nanoquant system from Roth, in accordance with the manufacturer instructions. BSA (bovine serum albumin) was used for protein calibration at concentrations ranging from 10 to 100 µg/ml.

SDS gel electrophoresis:

Electrophoretic separation of the proteins was done in a Multigel-Long electrophoresis chamber from Biometra with a denaturing, discontinuous 15% SDS-PAGE (polyacrylamide gel electrophoresis) according to Lämmli (Nature 277: 680-685, 1970). On top of this was poured a separation gel to a thickness of 1.5 mm: 7.5 ml acrylamide/bisacrylamide (30%, 0.9%), 3.8 ml 1.5 M tris/HCl, pH 8.4, 150 µl 10% SDS, 3.3 ml bidistilled water, 250 µl ammonium persulfate [10%], 9 µl TEMED (N,N,N',N'-tetramethylendiamine) and layered with 0.1% SDS until polymerization occurred. Then the collection gel was poured:

0.83 µl acrylamide/bisacrylamide (30%/0.9%), 630 µl 1 M tris/HCl, pH 6.8, 3.3 ml bidistilled water, 50 µl 10% SDS, 50 µl 10% ammonium persulfate, 5 µl TEMED.

Before being applied to the gel, a corresponding quantity of 4x sample buffer (200 mM tris, pH 6.8, 4% SDS, 100 mM DTT [dithiotreithol], 0.02% bromphenol blue, 20% glycerin) was added to the proteins, and denatured on a heat block at 100°C. After cooling off on ice, this was quickly centrifuged and applied to the gel. The same amounts of plasma or protein were used for each track (3 µl plasma or 25 µg total protein). Hydro-cooled electrophoresis was done at room temperature and at a constant 50 V. The protein gel marker from BioRad (Kaleidoscope Pre-stained Standard) was used as the standard length.

Western blot and Immunodetection:

Transfer of the proteins from SDS-PAGE to a PVDF (polyvinyl difluoride) membrane (Hybond-P, Amersham) was done using a semidry method according to Kyhse-Anderson (J. Biochem. Biophys. Methods 10:203-210, 1984) at room temperature and a constant amperage of 0.8 mA/cm2 for 1.5 hours. A tris/glycine buffer (39 mM Gly, 46 mM tris, 0.1% SDS, and 20% methanol) was used as the transfer buffer. In order to analyze electrophoretic transfer, both the post-blot gels and the blot membranes were stained after immunodetection using Coomassie (0.1% Coomassie G250, 45% methanol, 10% glacial acetic acid). The blot membrane was incubated after transfer in 1% skim milk powder/PBS for one hour at room temperature in order to saturate nonspecific bonds. After that, it was washed three times for 3 minutes with 0.1% Tween-20/PBS. All subsequent antibody incubations and washings were done using 0.1% Tween-20/PBS. Incubation with the primary antibody (goat anti-GFP, sc-5384, Santa Cruz Biotechnology) was done at a dilution of 1:1000 for 1 hour at room temperature. After that, it was washed 3 x 5 minutes , labeled with the

secondary antibody (donkey anti-goat IgG horseradish peroxidase, Santa Cruz Biotechnology) for 1 hour at room temperature at a dilution of 1:10,000. Detection was then done using the ECL system from Amersham in accordance with the manufacturer instructions.

Figures 18 to 20 show on, 3-µm paraffin sections, the inhibition of GFP expression after intravenous injection of specific anti-GFP directed dsRNA with anti-GFP immunoperoxidase stain. In the test run, anti-GFP directed dsRNA with a double-stranded region consisting of 22 nucleotide pairs without overhangs at the 3'-ends (D) and the corresponding nonspecific control dsRNA (B), as well as the specific anti-GFP directed dsRNA with a double-stranded region comprising 19 nucleotide pairs with 2nt overhangs at the 3'-ends (E) and the corresponding nonspecific control dsRNA (C) were applied in 12-hour rotations over 5 days. (F) received 1/50 of the dosage of Group D. Animals that received no dsRNA (A) and WT animals were also tested as a further control. Figure 18 shows the inhibition of GFP expression in kidney sections, Figure 19 in heart tissue sections, and Figure 20 in pancreas tissue. Western blot analyses of GFP expression in plasma and tissue are shown in Figures 21 to 23. Figure 21 shows the inhibition of GFP expression in plasma; Figure 22 in kidney tissue, and Figure 23 in heart tissue. The application of total protein isolates from various animals is shown in Figure 23. The same amounts of total protein were applied to each track. In the animals that received nonspecific control dsRNA (animals in Groups B and C), GFP expression was not reduced in comparison to animals that received no dsRNA whatsoever. Animals that received specific anti-GFP directed dsRNA that contained 2nt overhangs at the 3'-ends of both strands and a double-stranded region consisting of 19 nucleotide pairs showed significant inhibition of GFP expression in the tissues examined (heart, kidneys, pancreas,

and blood), compared with untreated animals (Figures 18 to 23). In animals in Groups D and F that were given specific anti-GFP directed dsRNA with smooth ends and a double-stranded region comprising 22 nucleotide pairs, only those animals that received the dsRNA in a dosage of 50 µg/kg body weight per day exhibited a specific inhibition of GFP expression, which, however, was less marked than in the animals in Group E.

Summary analysis of GFP inhibition in tissue sections and on Western blot show that inhibition of GFP expression is strongest in the blood and kidneys (Figures 18, 21, and 22).

V. Inhibition of gene expression of the EGF receptor with dsRNA as a therapeutic approach to forms of cancer characterized by EGFR overexpression or EGFR-induced proliferation:

The epidermal growth factor (=EGF) receptor (=EGFR) belongs to the tyrosin kinase receptors, transmembrane proteins with an intrinsic tyrosin kinase activity that are involved in the control of a series of cellular processes such as cell growth, cell differentiation, migratory processes, and cell vitality (overview in: Van der Geer et al., 1994). The EGFR family consists of 4 members, EGFR (ErbB1), HER2 (ErbB2), HER3 (ErbB3), and HER4 (ErbB4) with a transmembrane domain, a cystein-rich extracellular domain, and a catalytic intracellular domain. The EGFR sequence, a 170-kDa protein, has been known since 1984 (Ullrich et al., 1984).

EGFR is activated by peptide growth factors such as EGF, TGFα (transforming growth factor), amphiregulin, betacellulin, HB-EGF (heparin binding EGF-like growth factor), and neuregulins. Ligand binding induces the formation of homodimes or heterodimes with subsequent autophosphorylation of cytoplasmic tyrosine (Ullrich & Schlessinger, 1990; Alroy & Yarden, 1997). The

phosphorylated amino acids form the binding sites of numerous proteins that are involved in the proximal stages of signal transmission in a complex network. EGFR is involved in the most varied tumoral diseases, and is therefore an appropriate target for therapeutic approaches (Huang & Harari, 1999). The mechanisms that lead to aberrant EGFR activity may be related to overexpression, amplification, constitutive activation of mutant receptor forms, or autocrine loops (Voldberg et al., 1997). Overexpression of EGFR has been described for a series of tumors such as breast cancer (Walker & Dearing, 1999), non-minor lung cancer (Fontaninii et al., 1998), pancreatic cancer, colon cancer (Salomon et al., 1995), and glioblastoma (Rieske et al., 1998). For malignant glioblastoma, in particular, there have to date been no effective and specific therapeutic agents.

Example:

To detect the effectiveness of dsRNA in the specific inhibition of EGFR gene expression, U-87 MG cells (human glioblastoma cells), ECCAC (European Collection of Animal Cell Culture) No. 89081402 was used, and was transfected with the specific anti-EGF-receptor-directed dsRNA (sequence protocol SQ 51). After approximately 72 hours of incubation, the cells were harvested, the protein was isolated, and EGFR expression was analyzed by Western blot.

Test protocol:

dsRNA synthesis:

The individual RNA strands seen in the sequence protocols as well as their complementary individual strands were synthesized using an RNA synthesizer (Expedite 8909, Applied Biosystems, Weiterstadt, Germany), as well as by traditional chemical means. Purification of the raw synthesis products was then done with

the help of the HPLC. The NucleoPac PA-100, 9 x 250 column (Dionex) was used with 20 mM tris; 10 mM $NaClO_4$, pH 6.8, 10% acetonitrile was used as the low salt buffer, and 20 mM tris, 400 mM $NaClO_4$, pH 6.8, 10% acetonitrile were used as the high salt buffer. Flow was 3 ml per minute. Hybridization of the individual strands into a double-stranded was done by heating the stochiometric mixture of the individual strands in 10 mM sodium phosphate buffer, pH 6.8, 100 mM NaCl to 80-90°C and then allowing them to cool slowly over 6 hours to room temperature.

Seeding the cells:

All cell culturing was done under sterile conditions at an appropriate workstation (HS18/ Hera Safe, Kendro, Heraeus). Culturing of the U-87 MG cells was done in the incubator (CO_2-incubator T20, Hera Cell, Kendro, Heraeus) at 37°C, 5% CO_2 and saturated atmospheric humidity in DMEM (Dulbecco's modified eagle medium, Biochrom) with 10% FCS (fetal calf serum, Biochrom), 2 mM L-glutamine (Biochromone) mM sodium pyruvate (Biochrom), 1 x NEAA (nonessential amino acids, Biochrom), and penicillin/streptomycin (100 IU/100µg/ml, Biochrom). In order to maintain the cells in an exponential growth state, the cells were passaged every 3 days. 24 hours before dsRNA application by means of transfection, the cells were trypsinized (10 x trypsin/EDTA, Biochrom, Germany) and placed in a 6-well plate (6-well plates, Schubert & Weiss Laboratories, GmbH) in 1.5 µl growth medium.

DsRNA application in cultured U-87 MG cells:

Application of dsRNA was done by means of transfection using the OLIGOFECTAMINE™ reagent (Life Technologies) in accordance with the manufacturer instructions. Total transfection volume was 1 ml. First, the dsRNA was diluted in serum-free medium: 0.5µl of a 20 µM stock solution of specific anti-EGFR directed dsRNA and 9.5 µl of a 20 µM stock solution of nonspecific dsRNA (K1A/K2B)

diluted with 175 µl serum-free medium (200 nM dsRNA in the transfection incubate or 10 nM specific EGFR-dsRNA) per well. The OLIGOFECTAMINE™ reagent was also diluted in serum-free medium: 3 µl with 12 µl medium per well and then incubated for 10 minutes at room temperature. Then the diluted OLIGOFECTAMINE™ reagent was added to the medium of diluted dsRNA, mixed, and incubated for another 20 minutes at room temperature. The medium was changed during incubation. The cells were washed 1 x with 1 ml serum-free medium and continued to be incubated in the incubator with 800 µl serum-free medium until the dsRNA/OLIGOFECTAMINE™ reagent was added. After the addition of 200 µl dsRNA/OLIGOFECTAMINE™ reagent per well, the cells continued to be incubated in the incubator until protein isolation.

Protein isolation:

Approximately 72 hours after transfection, the cells were harvested and the protein was isolated. The medium was removed, and the cell monolayer was washed once with PBS. After the addition of 200 µl protein isolation buffer (1x "Complete" protease inhibitor, Roche, 50 mM HEPES, pH 7.5, 150 mM NaCl, 1 mM EDTA, 2.5 mM EGTA, 10% glycerin, 0.1% Tween-20, 1 mM DTT, 10 mM β-glycerine phosphate, 1 mM NaF, 0.1 mM Na_3VO_4) the cells were removed with the help of a cell scraper, incubated for 10 minutes on ice, transferred to an Eppendorf reagent vessel, and stored at -80°C for at least 30 minutes. After thawing, the lysate was homogenized at the third setting for 10 seconds with a disperser (DIAX 900, 6G disperser, Heidolph Instruments GmbH, Schwabach), incubated on ice for 10 minutes, and then centrifuged for 15 minutes at 14,000 xg at 4°C (3K30, Sigma). Protein determination according to Bradford was done on the supernatant fluid using the Roti-Nanoquant system from Roth (Roth GmbH, Karlsruhe) in accordance with the manufacturer's instructions. 200 µl protein solution at a suitable dilution is mixed with 800 µl 1x working solution, and extinction was

measured in semi-microcuvettes at 450 nm and 590 nm against distilled water in a Beckman spectrophotometer (DU 250). BSA dilutions were used for calibration (beaded BSA, Sigma).

SDS gel electrophoresis:

Electrophoretic separation of the proteins was done in a Multigel-Long electrophoresis chamber from Biometra with a denaturing, discontinuous 7.5% SDS-PAGE (polyacrylamide gel electrophoresis) according to Lämmli (Nature 277: 680-685, 1970). On top of this was poured a separation gel to a thickness of 1.5 mm: 3.75 ml acrylamide/bisacrylamide (30%, 0.9%), 3.8 ml 1 M tris/HCl, pH 8.4, 150 µl 10% SDS, 7.15 ml distilled water, 150 µl ammonium persulfate (10%), 9 µl TEMED (N,N,N',N'-tetramethylendiamine) and layered with 0.1 percent SDS until polymerization occurred. After that, the collection gel was poured: 0.83 ml acrylamide/bisacrylamide (30%/0.9%), 630 µl 1 M tris/HCl, pH 6.8, 3.4 ml distilled water, 50 µl 10% SDS, 50 µl 10% ammonium persulfate, 5 µl TEMED.

Before being applied to the gel, a quantity of 4x sample buffer (200 mM tris, pH 6.8, 4% SDS, 100 mM DTT [dithiotreithol], 0.02% bromphenol blue, 20% glycerin) was added to the proteins in a 1:3 ratio, and denatured at 100°C for 5 minutes. After cooling off on ice, this was quickly centrifuged and applied to the gel. The same amount of protein was used for each track (35 µg total protein). The hydro-cooled gel run was done at room temperature and at a constant 50 V. Kaleidoscope Prestained Standard (BioRad) was used as the standard length.

Western blot and Immunodetection:

Transfer of the proteins from SDS-PAGE to a PVDF (polyvinyl difluoride) membrane (Hybond-P, Amersham) was done using a semidry method according to Kyhse-Anderson (J. Biochem. Biophys. Methods 10:203-210, 1984) at room temperature and a constant 0.5

mA/cm^2 for 1.5 hours. A cathode buffer (30 mM tris, 40 mM glycine, 10% methanol, and 0.01% SDS, pH 9.4), anode buffer I (300 mM tris, pH 10.4, 10% methanol), and anode buffer II (30 mM tris, pH 10.4, 10% methanol) were used as the transfer buffers. Before assembling the blot stack with 3MM Whatman paper (Schleicher & Schüll) the gel was incubated in cathode buffer, and the PVDF membrane (previously for 30 seconds in 100% methanol) in anode buffer II (5 minutes): 2 layers of 3MM paper (anode buffer I), 1 layer 3MM paper (anode buffer II), PVDF membrane, gel, 3 layers 3MM paper (cathode buffer). To analyze electrophoretic transfer, both the post-blot gels and the blot membranes were stained after immunodetection using Coomassie (0.1% Coomassie G250, 45% methanol, 10% glacial acetic acid).

After transfer, the blot membrane was incubated in 1% skim milk powder/PBS/0.1% Tween-20 for one hour at room temperature. After that, it was washed three times for 3 minutes with 0.1% Tween-20/PBS. All subsequent antibody incubations and washings were done using 0.1% Tween-20/PBS. Incubation with the primary antibody (human EGFR extracellular domain, specific goat IgG, Catalogue No. AF231, R&D Systems) was done on a shaker for two hours at room temperature at a concentration of 1.5 µg/ml. After that it was washed 3 x 5 minutes and incubated for one hour at room temperature with the secondary antibody (labeled donkey anti-goat IgG horseradish peroxidase, Santa Cruz Biotechnology) at a dilution of 1:10,000. After washing (3 x 3 minutes in PBS/0.1% Tween-20) detection was immediately done by means of ECL reaction (enhanced chemoluminescence). To 18 ml of distilled water was pipetted 200 µl Solution A (250 mM luminol, Roth, dissolved in DMSO), 89 µl Solution B (90 mM p-coumaric acid, Sigma, dissolved in DMSO), and 2 ml 30% H_2O_2 solution. Depending on membrane size, 4-6 ml was pipetted directly onto the membrane, incubated for 1 minute at room temperature, and then layed immediately on x-ray film (Biomax MS, Kodak).

The sequences used here are contained in Table 3 below, as well as in sequence protocols SQ153, 157, 158, 168-173.

ES-7	SQ168 SQ169	(A) 5′- AACACCGCAGCAUGUCAAGAU -3′ (B) 3′- UUUUGUGGCGUCGUACAGUUC -5′	**2-19-2**
ES-8	SQ170 SQ171	(A) 5′- AAGUUAAAAUUCCCGUCGCUAU -3′ (B) 3′- CAAUUUUAAGGGCAGCGAUAGU -5′	**2^5-19-2^5**
ES2A/ ES5B	SQ172 SQ173	(A) 5′- AGUGUGAUCCAAGCUGUCCCAA -3′ (B) 3′- UUUCACACUAGGUUCGACAGGGUU -5′	**0-22-2**
K2	SQ157 SQ158	(A) 5′- ACAGGAUGAGGAUCGUUUCGCAUG -3′ (B) 3′- UCUGUCCUACUCCUAGCAAAGCGU -5′	**2-22-2**
K1A/ K2B	SQ153 SQ158	(A) 5′- ACAGGAUGAGGAUCGUUUCGCA -3′ (B) 3′- UCUGUCCUACUCCUAGCAAAGCGU -5′	**0-22-2**

Table 3

Inhibition of EGFR expression in U-87 MG glioblastoma cells:

24 hours after seeding the cells, they were transfected with 10 nM dsRNA as noted (oligofectamine). After 72 hours, the cells were harvested and the proteins isolated. Separation of the proteins was done in 7.5% SDS-PAGE. 35 µg total protein was applied to each track. The corresponding Western blot analysis may be seen in Figure 24, which shows that with the specific anti-EGFR-directed dsRNA with a 2nt overhang at the 3'-end of the antisense strand, EGFR expression after transfection in U-87 MG cells is significantly inhibited in comparison to the corresponding controls. This inhibition of expression of an endogenous gene by means of specific dsRNA confirms the results noted in Example II, of the inhibition of the expression of an

artificial gene inserted into the cell after transient transfection. The inhibition of EGFR expression mediated by ES-7 and ES-8 is notably smaller. The dsRNAs used in Figure 24 are shown in Table 3.

VI. Inhibiting expression of multi-drug resistance gene 1 (MDR1):

Test protocol:

In vitro detection of the blocking of MDR1 expression was done using the colon cancer cell line LS174T (ATCC - American Type Culture Collection; Tom et al., 1976). It is known of this cell line that expression of MDR1 is inducible by adding rifampicin to the culture medium (Geick et al., 2001). Transfection was done using a variety of commercially available transfection kits (Lipofectamine, Oligofectamine, both from Invitrogen; TransMessenger, Qiagen), of which the TransMessenger kit proved to be the most suitable for this cell line.

Four short double-stranded ribonucleic acids (R1-R4) were used to conduct the RNA interference experiments. Their sequences are shown in Table 4. The ribonucleic acids are homologous with segments of the coding sequence of MDR1 (sequence protocol SQ 30). Sequences R1-R3 consist of a 22-mer sense strand and a 24-mer antisense strand, whereby the resulting double strand exhibits a 2-nucleotide overhang at its 3'-end (0-22-2). Sequence R4 corresponds to R1; however it consists of a 19-mer double-stranded, each with 2-nucleotide overhangs at each 3'-end (2-19-2).

Name	Sequence protocol No.	Sequence	Position in Data bank-# AF016535
Seq	SQ141	5'- CCA UCU CGA AAA GAA GUU AAG A-3'	1320-1342
R1	SQ142	3'-UG GGU AGA GCU UUU CUU CAA UUC U-5'	1335-1318
Seq	SQ143	5'- UAU AGG UUC CAG GCU UGC UGU A-3'	2599-2621
R2	SQ152	3'-CG AUA UCC AAG GUC CGA ACG ACA U-5'	2621-2597
Seq	SQ144	5'- CCA GAG AAG GCC GCA CCU GCA U-3'	3778-3799
R3	SQ145	3'-UC GGU CUC UUC CGG CGU GGA CGU A-5'	3799-3776
Seq	SQ146	5'- CCA UCU CGA AAA GAA GUU AAG-3'	1320-1341
R4	SQ147	3'-UG GGU AGA GCU UUU CUU CAA U -5'	1339-1318
			Position in Data bank-# AF402779
K1A/	SQ153	5'- ACA GGA UGA GGA UCG UUU CGC A-3'	2829-2808
K2B	SQ158	3'-UC UGU CCU ACU CCU AGC AAA GCG U-5'	2808-2831

Table 4

The sequences shown in Table 4 are designated as sequences SQ141-147, 152, 153, and 158 in the sequence protocol. The dsRNA was in each case transfected into the cells as double assays at a concentration of 175 nM, which had on the day before been seeded in 12-well plates at 3.8 x 10^5 cells/well. For each transfection assay, 93.3 µl EC-R buffer (TransMessenger kits, Qiagen, Hilden) was mixed with 3.2 µl Enhancer R, and then 3.5 µl of the particular 20 µM dsRNA was added, mixed well, and incubated for 5 minutes at room temperature. After the addition of 6µl TransMessenger transfection reagent, the transfection

assay was mixed vigorously for 10 seconds, and then incubated for 10 minutes at room temperature. In the meantime, the medium was extracted from the cells, washed once with PBS (phosphate-buffered saline), and then 200 µl fresh medium without FCS was added to the cells in each well. After 10-minute incubation, 100 µl FCS-free medium was pipetted into each transfection assay, mixed, and the mixture was then pipetted drop by drop onto the cells (the dsRNA concentration of 175 µM relates to 400 µl medium total volume). The dsRNA/TransMessenger complexes were incubated with the cells for 4 hours at 37°C in FCS-free medium. The medium was then changed; the fresh medium contained 10 µM rifampin and 10% FCS. A non-specific dsRNA sequence that exhibits no homologies with the MDR1 gene sequence was used (K) as a control, and a MOCK transfection was conducted that contained all reagents except for dsRNA.

The cells were harvested after 24, 48, and 72 hours, and total RNA was extracted with the RNeasy mini kit from Qiagen. 10 µg total protein from each sample was then separated by electrophoresis on a 1% agarose-formaldehyde gel, blotted on a nylon membrane, and then hybridized as an internal control with specific probes that had been random-marked with 5'-α^{32}p-dCTP, first against MDR1, and after the blot had been stripped, against GAPDH, and then exposed on x-ray film.

The x-ray film was digitized (Image Master, VDS, Pharmacia) and quantified using Image-Quant software. At that time, adjustment between the MDR1-specific bands and the corresponding GAPDH bands was done.

Results:

Figs. 25 and 26 show Northern blots (Figs. 26a, 26a) with quantitative analysis of the MDR1-specific bands after adjustment with the corresponding GAPDH values (Figs. 25b, 26p).

A reduction in the MDR1-mRNA by as much as 55% was observed in comparison to the MOCK transfection, and by as much as 45% in comparison to the non-specific control transfection. After 48 hours there was a significant reduction in the MDR1-mRNA level in the dsRNA constructs designated as R1, R2, and R3 (Table 4). With the R4 dsRNA constructs, no significant reduction in comparison to the controls was observed after 48 hours (Figs. 26a and 26b). After 74 hours, there was a markedly stronger reduction in the MDR1-mRNA level with R1, R2, and R3 with the controls in comparison to the values at 48 hours (Figs. 25a and 26b). A significant decrease in the MDR1-mRNA level was seen at this time with R4 as well. Thus, the constructs with a 2nt overhang at the 3'-end of the antisense strand and a double-stranded region consisting of 22 nucleotide pairs reduces the MDR1-mRNA level more efficiently than do constructs with 2nt overhangs at the 3'-end of both strands (antisense strand and sent strand) and a double-stranded region consisting of 19 nucleotide pairs, relatively independent of the sequence region homologous to the MDR1 gene in each case (after 48 hours; Figure 26b). The results strengthen the findings in Example IV, which describe the inhibition of EGFR gene expression by means of specific dsRNAs after transfection in U-87 MG cells.

Transfection efficiency was determined in a separate experiment with the help of a DNA oligonucleotide marked with Texas red (TexRed-A[GATC]$_5$T; also transfected with 175 nM) (Figs. 27a, 27b; 400x enlargement, 48 hours after transfection). Transfection efficiency was approximately 50% on the basis of red fluorescent cells in comparison to total cell number. If one takes the transfection rate of cells of approximately 50% into consideration, then it seems reasonable to conclude that given the observed decrease in the MDR1-mRNA level by approximately 45-55% (compared with the controls), that MDR1-mRNA was almost

completely and specifically broken down in all cells that were successfully transfected with specific dsRNA.

Literature:

Alroy I & Yarden Y (1997): The Erb signalling network in embryogenesis and oncogenesis: signal deversification through combinatorial ligand-receptor interactions. FEBS Letters 410: 83-86.

Bass,B.L., 2000. Double-stranded RNA as a template for gene silencing. Cell 101, 235-238.

Bosher,J.M. and Labouesse,M., 2000. RNA interference: genetic wand and genetic watchdog. Nature Cell Biology 2, E31-E36.

Bradford MM (1976): Rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. Anal. Biochem. 72: 248-254.

Caplen,N.J., Fleenor,J., Fire,A., and Morgan,R.A., 2000. dsRNA-mediated gene silencing in cultured *Drosophila* cells: a tissue culture model for the analysis of RNA interference. Gene 252, 95-105.

Clemens,J.C., Worby,C.A., Simonson-Leff,N., Muda,M., Maehama,T., Hemmings,B.A., and Dixon,J.E., 2000. Use of double-stranded RNA interference in *Drosophila* cell lines to dissect signal transduction pathways. *Proc.Natl.Acad.Sci.USA* 97, 6499-6503.

Cobleigh MA, Vogel CL, Tripathy D, Robert NJ, Scholl S, Fehrenbacher L, Wolter JM, Paton V, Shak S, Lieberman G & Slamon DJ (1999): Multinational study of the efficacy and safety of humanized anti-HER2 monoclonal antibody in women who have HER2-overexpressing metastatic breast cancer that has progressed after chemotherapy for metastatic disease. Journal of Clinical Oncology 17: 2639-2648.

Ding,S.W., 2000. RNA silencing. Curr. Opin. Biotechnol. 11, 152-156.

Fire,A., Xu,S., Montgomery,M.K., Kostas,S.A., Driver,S.E., and Mello,C.C., 1998. Potent and specific genetic interference by double-stranded RNA in *Caenorhabditis elegans*. Nature 391, 806-811.

Fire,A., 1999. RNA-triggered gene silencing. Trends Genet. 15, 358-363.

Freier,S.M., Kierzek,R., Jaeger,J.A., Sugimoto,N., Caruthers,M.H., Neilson,T., and Turner,D.H., 1986. Improved free-energy parameters for prediction of RNA duplex stability. Proc. Natl. Acad. Sci. USA 83, 9373-9377 .

Geick, A., Eichelbaum, M., Burk, O. (2001). Nuclear receptor response elements mediate induction of intestinal MDR1 by rifampin. J. Biol. Chem. 276 (18), 14581-14587.

Fontanini G, De Laurentiis M, Vignati S, Chine S, Lucchi M, Silvestri V, Mussi A, De Placido S, Tortora G, Bianco AR, Gullick W, Angeletti CA, Bevilaqua G & Ciardiello F (1998): Evaluation of epidermal growth factor-related growth factors and receptors and of neoangiogenesis in completely resected stage I-IIIA non-small-cell lung cancer: amphiregulin and microvessel count are independent prognostic factors of survival. Clinical Cancer Research 4: 241-249.

Hammond,S.M., Bernstein,E., Beach,D., and Hannon,G.J., 2000. An RNA-directed nuclease mediates post-transcriptional gene silencing in *Drosophila* cells. Nature 404, 293-296.

Higgins, C.F. (1995). The ABC of channel regulation. Cell, 82, 693-696.

Hadjantonakis AK, Gertsenstein M, Ikawa M, Okabe M & Nagy A (1993): Generating green fluorescent mice by germline transmission of green fluorescent ES cells. Mech. Dev. 76: 79-90.

Hadjantonakis AK, Gertsenstein M, Ikawa M, Okabe M & Nagy A (1998): Non-invasive sexing of preimplantation mammalian embryos. Nature Genetics 19: 220-222.

Kyhse-Anderson J (1984): Electroblotting of multiple gels: A simple apparatus without buffer tank for rapid transfer of proteins from polyacrylamide to nitrocellulose. J. Biochem. Biophys. Methods 10: 203-210.

Lämmli UK (1970): Cleavage of structural proteins during the assembly of the head of bacteriophage T4. Nature 277: 680-685.

Loo, T.W., and Clarke, D.M. (1999) *Biochem. Cell Biol.* 77, 11-23.

Huang SM & Harari PM (1999): Epidermal growth factor receptor inhibition in cancer therapy: biology, rationale and preliminary clinical results. Investigational New Drugs 17: 259-269.

Limmer,S., Hofmann,H.-P., Ott,G., and Sprinzl,M., 1993. The 3'-terminal end (NCCA) of tRNA determines the structure and stability of the aminoacyl acceptor stem. Proc. Natl. Acad. Sci. USA 90 , 6199-6202.

Montgomery,M.K. and Fire,A., 1998. Double-stranded RNA as a mediator in sequence-specific genetic silencing and co-suppression. Trends Genet. 14, 255-258.

Montgomery,M.K., Xu,S., and Fire,A., 1998. RNA as a target of double-stranded RNA-mediated genetic interference in *Caenorhabditis elegans*. Proc. Natl. Acad. Sci. USA 95, 15502-15507.

Rieske P, Kordek R, Bartkowiak J, Debiec-Rychter M, Bienhat W & Liberski PP (1998): A comparative study of epidermal growth factor (EGFR) and mdm2 gene amplification and protein immunoreactivity in human glioblastomas. Polish Journal of Pathology 49: 145-149.

Robert, J. (1999). Multidrug resistance in oncology: diagnostic and therapeutic approaches. Europ J Clin Invest 29, 536-545.

Stavrovskaya, A.A. (2000) Biochemistry (Moscow) 65 (1), 95-106.

Salomon DS, Brandt R, Ciardiello F & Normanno N (1995): Epidermal growth factor related peptides and their receptors in human malignancies: Critical Reviews in Oncology and Haematology 19: 183-232.

Tom, B.H., Rutzky, L.P., Jakstys, M.M., Oyasu, R., Kaye, C.I., Kahan, B.D. (1976), In vitro, 12, 180-191.

Tsuruo, T., Iida, H., Tsukagoshi, S., Sakurai, Y. (1981). Overcoming of vincristine resistance in P388 leukemia in vivo and in vitro through enhanced cytotoxicity of vincristine and vinblastine by verapamil. *Cancer Res*, 41, 1967-72.

Ui-Tei,K., Zenno,S., Miyata,Y., and Saigo,K., 2000. Sensitive assay of RNA interference in *Drosophila* and Chinese hamster cultured cells using firefly luciferase gene as target. FEBS Lett. 479, 79-82.

Ullrich A, Coussens L, Hayflick JS, Dull TJ, Gray A, Tam AW, Lee J, Yarden Y, Liebermann TA, Schlessinger J et al. (1984): Human epidermal growth factor receptor cDNA sequences and aberrant expression of the amplified gene in A431 epidermoid carcinoma cells. Nature 309: 418-425.

Ullrich A & Schlessinger J (1990): Signal transduction by receptors with tyrosine kinase activity. Cell 61: 203-212.

Van der Geer P, Hunter T & Linberg RA (1994): Receptor protein-tyrosine kinases and their signal transduction pathways. Annual review in Cell Biology 10: 251-337.

Voldborg BR, Damstrup L, Spang-Thopmsen M & Poulsen HS (1997): Epidermal growth factor Receptor (EGFR) and EGFR mutations, function and possible role in clinical trials. Annuals of Oncology 8: 1197-1206.

Walker RA & Dearing SJ (1999): Expression of epidermal growth factor receptor mRNA and protein in primary breast carcinomas. Breast Cancer Research Treatment 53: 167-176.

Zamore,P.D., Tuschl,T., Sharp,P.A., and Bartel,D.P., 2000. RNAi: double-stranded RNA directs the ATP-dependent cleavage of mRNA at 21 to 23 nucleotide intervals. Cell 101 , 25-33.

Zor T & Selinger Z (1996): Linearization of the Bradford protein assay increases its sensitivity: theoretical and experimental studies. Anal. Biochem. 236: 302-308.

SEQUENCE PROTOCOL

<110> Ribopharma AG

<120> Method to inhibit expression of a target gene

<130>

<140>
<141>

<160> 142

<170> PatentIn Ver. 2.1

<210> 1
<211> 2955
<212> DNA
<213> Homo sapiens

<300>
<302> Eph A1
<310> NM00532

<300>
<302> ephrin A1
<310> NM00532

<400> 1
atggagcggc gctggcccct ggggctaggg ctggtgctgc tgctctgcgc cccgctgccc 60
ccgggggcgc gcgccaagga agttactctg atggacacaa gcaaggcaca gggagagctg 120
ggctggctgc tggatccccc aaaagatggg tggagtgaac agcaacagat actgaatggg 180
acaccccttct acatgtacca ggactgccca atgcaaggac gcagagacac tgaccactgg 240
cttcgctcca attggatcta ccgcggggag gaggcttccc gcgtccacgt ggagctgcag 300
ttcaccgtgc gggactgcaa gagtttccct gggggagccg ggcctctggg ctgcaaggag 360
accttcaacc ttctgtacat ggagagtgac caggatgtgg gcattcagct ccgacggccc 420
ttgttccaga aggtaaccac ggtggctgca gaccagagct tcaccattcg agaccttgcg 480
tctggctccg tgaagctgaa tgtggagcgc tgctctctgg gccgcctgac ccgccgtggc 540
ctctacctcg ctttccacaa cccgggtgcc tgtgtggccc tggtgtctgt ccgggtcttc 600
taccagcgct gtcctgagac cctgaatggc ttggcccaat tcccagacac tctgcctggc 660
cccgctgggt tggtggaagt ggcgggcacc tgcttgcccc acgcgcgggc cagccccagg 720
ccctcaggtg caccccgcat gcactgcagc cctgatggcg agtggctggt gcctgtagga 780
cggtgccact gtgagcctgg ctatgaggaa ggtggcagtg gcgaagcatg tgttgcctgc 840
cctagcggct cctaccggat ggacatggac acaccccatt gtctcacgtg cccccagcag 900
agcactgctg agtctgaggg ggccaccatc tgtacctgtg agagcggcca ttacagagct 960
cccggggagg gccccaggt ggcatgcaca ggtccccctt cggccccccg aaacctgagc 1020
ttctctgcct cagggactca gctctccctg cgttgggaac ccccagcaga tacgggggga 1080
cgccaggatg tcagatacag tgtgaggtgt tcccagtgtc agggcacagc acaggacggg 1140
gggccctgcc agccctgtgg ggtgggcgtg cacttctcgc cgggggcccg ggcgctcacc 1200
acacctgcag tgcatgtcaa tggccttgaa ccttatgcca actacacctt taatgtggaa 1260
gcccaaaatg gagtgtcagg gctgggcagc tctggccatg ccagcacctc agtcagcatc 1320
agcatggggc atgcagagtc actgtcaggc ctgtctctga gactggtgaa gaaagaaccg 1380
aggcaactag agctgacctg ggcggggtcc cggccccgaa gccctggggc gaacctgacc 1440
tatgagctgc acgtgctgaa ccaggatgaa gaacggtacc agatggttct agaacccagg 1500
gtcttgctga cagagctgca gcctgacacc acatacatcg tcagagtccg aatgctgacc 1560
ccactgggtc ctggcccttt ctccctgat catgagtttc ggaccagccc accagtgtcc 1620
aggggcctga ctggaggaga gattgtagcc gtcatctttg ggctgctgct tggtgcagcc 1680
ttgctgcttg ggattctcgt tttccggtcc aggagagccc agcggcagag gcagcagagg 1740
cacgtgaccg cgccaccgat gtggatcgag aggacaagct gtgctgaagc cttatgtggt 1800

acctccaggc atacgaggac cctgcacagg gagccttgga ctttacccgg aggctggtct 1860
aattttcctt cccgggagct tgatccagcg tggctgatgg tggacactgt cataggagaa 1920
ggagagtttg gggaagtgta tcgagggacc ctcaggctcc ccagccagga ctgcaagact 1980
gtggccatta agaccttaaa agacacatcc ccaggtggcc agtggtggaa cttccttcga 2040
gaggcaacta tcatgggcca gtttagccac ccgcatattc tgcatctgga aggcgtcgtc 2100
acaaagcgaa agccgatcat gatcatcaca gaatttatgg agaatgcagc cctggatgcc 2160
ttcctgaggg agcgggagga ccagctggtc cctgggcagc tagtggccat gctgcagggc 2220
atagcatctg gcatgaacta cctcagtaat cacaattatg tccaccggga cctggctgcc 2280
agaaacatct tggtgaatca aaacctgtgc tgcaaggtgt ctgactttgg cctgactcgc 2340
ctcctggatg actttgatgg cacatacgaa acccagggag gaaagatccc tatccgttgg 2400
acagcccctg aagccattgc ccatcggatc ttcaccacag ccagcgatgt gtggagcttt 2460
gggattgtga tgtgggaggt gctgagcttt ggggacaagc cttatgggga gatgagcaat 2520
caggaggtta tgaagagcat tgaggatggg taccggttgc cccctcctgt ggactgccct 2580
gcccctctgt atgagctcat gaagaactgc tgggcatatg accgtgcccg ccggccacac 2640
ttccagaagc ttcaggcaca tctggagcaa ctgcttgcca acccccactc cctgcggacc 2700
attgccaact ttgaccccag ggtgactctt cgcctgccca gcctgagtgg ctcagatggg 2760
atcccgtatc gaaccgtctc tgagtggctc gagtccatac gcatgaaacg ctacatcctg 2820
cacttccact cggctgggct ggacaccatg gagtgtgtgc tggagctgac cgctgaggac 2880
ctgacgcaga tgggaatcac actgcccggg caccagaagc gcattctttg cagtattcag 2940
ggattcaagg actga 2955

<210> 2
<211> 3042
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin A2
<310> XM002088

<400> 2
gaagttgcgc gcaggccggc gggcgggagc ggacaccgag gccggcgtgc aggcgtgcgg 60
gtgtgcggga gccgggctcg gggggatcgg accgagagcg agaagcggcg catggagctc 120
caggcagccc gcgcctgctt cgccctgctg tggggctgtg cgctggccgc ggccgcggcg 180
gcgcagggca aggaagtggt actgctggac tttgctgcag ctggaggggg gctcggctgg 240
ctcacacacc cgtatggcaa agggtgggac ctgatgcaga acatcatgaa tgacatgccg 300
atctacatgt actccgtgtg caacgtgatg tctggcgacc aggacaactg gctccgcacc 360
aactgggtgt accgaggaga ggctgagcgt atcttcattg agctcaagtt tactgtacgt 420
gactgcaaca gcttccctgg tggcgccagc tcctgcaagg agactttcaa cctctactat 480
gccgagtcgg acctggacta cggcaccaac ttccagaagc gcctgttcac caagattgac 540
accattgcgc ccgatgagat caccgtcagc agcgacttcg aggcacgcca cgtgaagctg 600
aacgtggagg agcgctccgt ggggccgctc acccgcaaag gcttctacct ggccttccag 660
gatatcggtg cctgtgtggc gctgctctcc gtccgtgtct actacaagaa gtgccccgag 720
ctgctgcagg gcctggccca cttccctgag accatcgccg gctctgatgc accttccctg 780
gccactgtgg ccggcacctg tgtggaccat gccgtggtgc caccgggggg tgaagagccc 840
cgtatgcact gtgcagtgga tggcgagtgg ctggtgccca ttgggcagtg cctgtgccag 900
gcaggctacg agaaggtgga ggatgcctgc caggcctgct cgccttggatt ttttaagttt 960
gaggcatctg agagcccctg cttggagtgc cctgagcaca cgctgccatc ccctgagggt 1020
gccacctcct gcgagtgtga ggaaggcttc ttccgggcac ctcaggaccc agcgtcgatg 1080
ccttgcacac gaccccctc cgccccacac tacctcacag ccgtgggcat gggtgccaag 1140
gtggagctgc gctggacgcc ccctcaggac agcggggggc gcgaggacat tgtctacagc 1200
gtcacctgcg aacagtgctg gcccgagtct ggggaatgcg ggccgtgtga ggccagtgtg 1260
cgctactcgg agcctcctca cggactgacc cgcaccagtg tgacagtgag cgacctggag 1320
ccccacatga actacacctt cacccgtgag gcccgcaatg gcgtctcagg cctggtaacc 1380
agccgcagct tccgtactgc cagtgtcagc atcaaccaga cagagccccc caaggtgagg 1440
ctggagggcc gcagcaccac ctcgcttagc gtctcctgga gcatccccgc gccgcagcag 1500
agccgagtgt ggaagtacga ggtcacttac cgcaagaagg gagacctccaa cagctacaat 1560
gtgcgccgca ccgagggttt ctccgtgacc ctggacgacc tggccccaga caccacctac 1620
ctggtccagg tgcaggcact gacgcaggag ggccaggggg ccggcagcaa ggtgcacgaa 1680

ttccagacgc tgtccccgga gggatctggc aacttggcgg tgattggcgg cgtggctgtc 1740
ggtgtggtcc tgcttctggt gctggcagga gttggcttct ttatccaccg caggaggaag 1800
aaccagcgtg cccgccagtc cccggaggac gtttacttct ccaagtcaga acaactgaag 1860
cccctgaaga catacgtgga ccccacacca tatgaggacc ccaaccaggc tgtgttgaag 1920
ttcactaccg agatccatcc atcctgtgtc actcggcaga aggtgatcgg agcaggagag 1980
tttggggagg tgtacaaggg catgctgaag acatcctcgg ggaagaagga ggtgccggtg 2040
gccatcaaga cgctgaaagc cggctacaca gagaagcagc gagtggactt cctcggcgag 2100
gccggcatca tgggccagtt cagccaccac aacatcatcc gcctagaggg cgtcatctcc 2160
aaatacaagc ccatgatgat catcactgag tacatggaga atggggccct ggacaagttc 2220
cttcgggaga aggatggcga gttcagcgtg ctgcagctgg tgggcatgct gcggggcatc 2280
gcagctggca tgaagtacct ggccaacatg aactatgtgc accgtgacct ggctgcccgc 2340
aacatcctcg tcaacagcaa cctggtctgc aaggtgtctg actttggcct gtcccgctg 2400
ctggaggacg accccgaggc cacctacacc accagtggcg gcaagatccc catccgctgg 2460
accgccccgg aggccatttc ctaccggaag ttcacctctg ccagcgacgt gtggagcttt 2520
ggcattgtca tgtgggaggt gatgacctat ggcgagcggc cctactggga gttgtccaac 2580
cacgaggtga tgaaagccat caatgatggc ttccggctcc ccacacccat ggactgcccc 2640
tccgccatct accagctcat gatgcagtgc tggcagcagg agcgtgcccg ccgccccaag 2700
ttcgctgaca tcgtcagcat cctggacaag ctcattcgtg cccctgactc cctcaagacc 2760
ctggctgact ttgacccccg cgtgtctatc cggctcccca gcacgagcgg ctcggagggg 2820
gtgccctcc gcacggtgtc cgagtggctg gagtccatca agatgcagca gtatacggag 2880
cacttcatgg cggccggcta cactgccatc gagaaggtgg tgcagatgac caacgacgac 2940
atcaagagga ttggggtgcg gctgccccgc caccagaagc gcatcgccta cagcctgctg 3000
ggactcaagg accaggtgaa cactgtgggg atccccatct ga 3042

<210> 3
<211> 2953
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin A3
<310> NM005233

<400> 3
atggattgtc agctctccat cctcctcctt ctcagctgct ctgttctcga cagcttcggg 60
gaactgattc cgcagccttc caatgaagtc aatctactgg attcaaaaac aatttcaggg 120
gagctgggct ggatctctta tccatcacat gggtgggaag agatcagtgg tgtggatgaa 180
cattacacac ccatcaggac ttaccaggtg tgcaatgtca tggaccacag tcaaaacaat 240
tggctgagaa caaactgggt ccccaggaac tcagctcaga agatttatgt ggagctcaag 300
ttcactctac gagactgcaa tagcattcca ttggttttag gaacttgcaa ggagacattc 360
aacctgtact acatggagtc tgatgatgat catggggtga aatttcgaga gcatcagttt 420
acaaagattg acaccattgc agctgatgaa agtttcactc aaatggatct tggggaccgt 480
attctgaagc tcaacactga gattagagaa gtaggtcctg tcaacaagaa gggattttat 540
ttggcatttc aagatgttgg tgcttgtgtt gccttggtgt ctgtgagagt atacttcaaa 600
aagtgcccat ttacagtgaa gaatctggct atgtttccag acacggtacc catggactcc 660
cagtccctgg tggaggttag agggtcttgt gtcaacaatt ctaaggagga agatcctcca 720
aggatgtact gcagtacaga aggcgaatgg cttgtaccca ttggcaagtg ttcctgcaat 780
gctggctatg aagaaagagg ttttatgtgc caagcttgtc gaccaggttt ctacaaggca 840
ttggatggta atatgaagtg tgctaagtgc ccgcctcaca gttctactca ggaagatggt 900
tcaatgaact gcaggtgtga gaataattac ttccgggcag acaaagaccc tccatccatg 960
gcttgtaccc gacctccatc ttcaccaaga aatgttatct ctaatataaa cgagacctca 1020
gttatcctgg actggagttg gcccctggac acaggaggcc ggaaagatgt taccttcaac 1080
atcatatgta aaaaatgtgg gtggaatata aaacagtgtg agccatgcag cccaaatgtc 1140
cgcttcctcc ctcgacagtt tggactcacc aacaccacgg tgacagtgac agaccttctg 1200
gcacatacta actacacctt tgagattgat gccgttaatg gggtgtcaga gctgagctcc 1260
ccaccaagac agttgctgtc ggtcagcatc acaactaatc aggctgctcc atcacctgtc 1320
ctgacgatta agaaagatcg gacctccaga aatagcatct ctttgtcctg gcaagaacct 1380
gaacatccta atgggatcat attggactac gaggtcaaat actatgaaaa gcaggaacaa 1440
gaaacaagtt ataccattct gagggcaaga ggcacaaatg ttaccatcag tagcctcaag 1500

cctgacacta tatacgtatt ccaaatccga gcccgaacag ccgctggata tgggacgaac 1560
agccgcaagt ttgagtttga aactagtcca gactctttct ccatctctgg tgaaagtagc 1620
caagtggtca tgatogccat ttcagcggca gtagcaatta ttctcctcac tgttgtcatc 1680
tatgttttga ttgggaggtt ctgtggctat aagtcaaaac atgggggcaga tgaaaaaaga 1740
cttcattttg gcaatgggca tttaaaactt ccaggtctca ggacttatgt tgacccacat 1800
acatatgaag accctaccca agctgttcat gagtttgcca aggaattgga tgccaccaac 1860
atatccattg ataaagttgt tggagcaggt gaatttggag aggtgtgcag tggtcgctta 1920
aaacttcctt caaaaaaaga gatttcagtg gccattaaaa ccctgaaagt tggctacaca 1980
gaaaagcaga ggagagactt cctgggagaa gcaagcatta tgggacagtt tgaccacccc 2040
aatatcattc gactggaagg agttgttatcc aaaagtaagc cagttatgat tgtcacagaa 2100
tacatggaga atggttcctt ggatagtttc ctacgtaaac acgatgccca gtttactgtc 2160
attcagctag tggggatgct tcgagggata gcatctggca tgaagtacct gtcagacatg 2220
ggctatgttc accgagacct cgctgctcgg aacatcttga tcaacagtaa cttggtgtgt 2280
aaggtttctg atttcggact ttcgcgtgtc ctggaggatg acccagaagc tgcttataca 2340
acaagaggag ggaagatccc aatcaggtgg acatcaccag aagctatagc ctaccgcaag 2400
ttcacgtcag ccagcgatgt atggagttat gggattgttc tctgggaggt gatgtcttat 2460
ggagagagac catactggga gatgtccaat caggatgtaa ttaaagctgt agatgagggc 2520
tatcgactgc caccccccat ggactgccca gctgccttgt atcagctgat gctggactgc 2580
tggcagaaag acaggaacaa cagacccaag tttgagcaga ttgttagtat tctggacaag 2640
cttatccgga atcccggcag cctgaagatc atcaccagtg cagccgcaag gccatcaaac 2700
cttcttctgg accaaagcaa tgtggatatc tctaccttcc gcacaacagg tgactggctt 2760
aatggtgtcc ggacagcaca ctgcaaggaa atcttcacgg gcgtggagta cagttcttgt 2820
gacacaatag ccaagatttc cacagatgac atgaaaaagg ttggtgtcac cgtggttggg 2880
ccacagaaga agatcatcag tagcattaaa gctctagaaa cgcaatcaaa gaatggccca 2940
gttcccgtgt aaa 2953

<210> 4
<211> 2784
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin A4
<310> XM002578

<400> 4
atggatgaaa aaaatacacc aatccgaacc taccaagtgt gcaatgtgat ggaacccagc 60
cagaataact ggctacgaac tgattggatc acccgagaag gggctcagag ggtgtatatt 120
gagattaaat tcaccttgag ggactgcaat agtcttccgg gcgtcatggg gacttgcaag 180
gagacgttta acctgtacta ctatgaatca gacaacgaca aagagcgttt catcagagag 240
aaccagtttg tcaaaattga caccattgct gctgatgaga gcttcaccca agtggacatt 300
ggtgacagaa tcatgaagct gaacaccgag atccgggatg tagggccatt aagcaaaaag 360
gggttttacc tggcttttca ggatgtgggg gcctgcatcg ccctggtatc agtccgtgtg 420
ttctataaaa agtgtccact cacagtccgc aatctggccc agtttcctga caccatcaca 480
ggggctgata cgtcttccct ggtggaagtt cgaggctcct gtgtcaacaa ctcagaagag 540
aaagatgtgc caaaaatgta ctgtggggca gatggtgaat ggctggtacc cattggcaac 600
tgcctatgca acgctgggca tgaggagcgg agcggagaat gccaagcttg caaaattgga 660
tattacaagg ctctctccac ggatgccacc tgtgccaagt gcccacccca cagctactct 720
gtctgggaag gagccacctc gtgcacctgt gaccgaggct ttttcagagc tgacaacgat 780
gctgcctcta tgccctgcac ccgtccacca tctgctcccc tgaacttgat ttcaaatgtc 840
aacgagacat ctgtgaactt ggaatggagt agccctcaga atacaggtgg ccgccaggac 900
atttcctata atgtggtatg caagaaatgt ggagctggtg accccagcaa gtgccgaccc 960
tgtggaagtg gggtccacta cacccacag cagaatggct tgaagaccac caaagtctcc 1020
atcactgacc tcctagctca taccaattac acctttgaaa tctgggctgt gaatggagtg 1080
tccaaatata accctaaccc agaccaatca gtttctgtca ctgtgaccac caaccaagca 1140
gcaccatcat ccattgcttt ggtccaggct aaagaagtca caagatacag tgtggcactg 1200
gcttggctgg aaccagatcg gcccaatggg gtaatcctgg aatatgaagt caagtattat 1260
gagaaggatc agaatgagcg aagctatcgt atagttcgga cagctgccag gaacacagat 1320
atcaaaggcc tgaaccctct cacttcctat gttttccacg tgcgagccag gacagcagct 1380

ggctatggag acttcagtga gcccttggag gttacaacca acacagtgcc ttcccggatc 1440
attggagatg gggctaactc cacagtcctt ctggtctctg tctcgggcag tgtggtgctg 1500
gtggtaattc tcattgcagc ttttgtcatc agccggagac ggagtaaata cagtaaagcc 1560
aaacaagaag cggatgaaga gaaacatttg aatcaaggtg taagaacata tgtggacccc 1620
tttacgtacg aagatcccaa ccaagcagtg cgagagtttg ccaaagaaat tgacgcatcc 1680
tgcattaaga ttgaaaaagt tataggagtt ggtgaatttg gtgaggtatg cagtgggcgt 1740
ctcaaagtgc ctggcaagag agagatctgt gtggctatca agactctgaa agctggttat 1800
acagacaaac agaggagaga cttcctgagt gaggccagca tcatgggaca gtttgacctat 1860
ccgaacatca ttcacttgga aggcgtggtc actaaatgta aaccagtaat gatcataaca 1920
gagtacatgg agaatggctc ctttgatgca ttcctcagga aaaatgatgg cagatttaca 1980
gtcattcagc tggtgggcat gcttcgtggc attgggtctg ggatgaagta tttatctgat 2040
atgagctatg tgcatcgtga tctggccgca cggaacatcc tggtgaacag caacttggtc 2100
tgcaaagtgt ctgattttgg catgtcccga gtgcttgagg atgatccgga agcagcttac 2160
accaccaggg gtggcaagat tcctatccgg tggactgcgc cagaagcaat tgcctatcgt 2220
aaattcacat cagcaagtga tgtatggagc tatggaatcg ttatgtggga agtgatgtcg 2280
tacggggaga ggccctattg ggatatgtcc aatcaagatg tgattaaagc cattgaggaa 2340
ggctatcggt taccccctcc aatggactgc cccattgcgc tccaccagct gatgctagac 2400
tgctggcaga aggagaggag cgacaggcct aaatttgggc agattgtcaa catgttggac 2460
aaactcatcc gcaaccccaa cagcttgaag aggacaggga cggagagctc cagacctaac 2520
actgccttgt tggatccaag ctcccctgaa ttctctgctg tggtatcagt gggcgattgg 2580
ctccaggcca ttaaaatgga ccggtataag gataacttca cagctgctgg ttataccaca 2640
ctagaggctg tggtgcacgt gaaccaggag gacctggcaa gaattggtat cacagccatc 2700
acgcaccaga ataagatttt gagcagtgtc caggcaatgc gaacccaaat gcagcagatg 2760
cacggcagaa tggttcccgt ctga 2784

<210> 5
<211> 2997
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin A7
<310> XM004485

<400> 5
atggtttttc aaactcggta cccttcatgg attattttat gctacatctg gctgctccgc 60
tttgcacaca caggggaggc gcaggctgcg aaggaagtac tactgctgga ttctaaagca 120
caacaaacag agttggagtg gatttcctct ccacccaatg ggtgggaaga aattagtggt 180
ttggatgaga actatacccc gatacgaaca taccaggtgt gccaagtcat ggagccccaac 240
caaaacaact ggctgcggac taactggatt tccaaaggca atgcacaaag gatttttgta 300
gaattgaaat tcaccctgag ggattgtaac agtcttcctg gagtactggg aacttgcaag 360
gaaacattta atttgtacta ttatgaaaca gactatgaca ctggcaggaa tataagagaa 420
aacctctatg taaaaataga caccattgct gcagatgaaa gttttaccca aggtgacctt 480
ggtgaaagaa agatgaagct taacactgag gtgagagaga ttggaccttt gtccaaaaag 540
ggattctatc ttgcctttca ggatgtaggg gcttgcatag ctttggtttc tgtcaaagtg 600
tactacaaga agtgctggtc cattattgag aacttagcta tctttccaga tacagtgact 660
ggttcagaat tttcctcttt agtcgaggtt cgagggacat gtgtcagcag tgcaggaaga 720
gaagcggaaa acgcccccag gatgcactgc agtgcagaag gagaatggtt agtgcccatt 780
ggaaaatgta tctgcaaagc aggctaccag caaaaaggag acacttgtga accctgtggc 840
cgtgggttct acaagtcttc ctctcaagat cttcagtgct ctcgttgtcc aactcacagt 900
ttttctgata aagaaggctc ctccagatgt gaatgtgaag atgggtatta cagggctcca 960
tctgacccac catacgttgc atgcacaagg cctccatctg cacccacagaa cctcattttc 1020
aacatcaacc aaaccacagt aagtttggaa tggagtcctc ctgcagacaa tgggggaaga 1080
aacgatgtga cctacagaat attgtgtaag cggtgcagtt gggagcaggg cgaatgtgtt 1140
ccctgtggga gtaacattgg atacatgccc cagcagactg gattagagga taactatgtc 1200
actgtcatgg acctgctagc ccacgctaat tatacttttg aagttgaagc tgtaaatgga 1260
gttctcgact taagccgatc ccagaggctc tttgctgctg tcagtatcac cactggtcaa 1320
gcagctccct cgcaagtgag tggagtaatg aaggagagag tactgcagcg gagtgtcgag 1380
ctttcctggc aggaaccaga gcatcccaat ggagtcatca cagaatatga aatcaagtat 1440

tacgagaaag atcaaaggga acggacctac tcaacagtaa aaaccaagtc tacttcagcc 1500
tccattaata atctgaaacc aggaacagtg tatgttttcc agattcgggc ttttactgct 1560
gctggttatg gaaattacag tcccagactt gatgttgcta cactagagga agctacaggt 1620
aaaatgtttg aagctacagc tgtctccagt gaacagaatc ctgttattat cattgctgtg 1680
gttgctgtag ctgggaccat cattttggtg ttcatggtct ttggcttcat cattgggaga 1740
aggcactgtg gttatagcaa agctgaccaa gaagggcgatg aagagcttta ctttcatttt 1800
aaatttccag gcaccaaaac ctacattgac cctgaaacct atgaggaccc aaatagagct 1860
gtccatcaat tcgccaagga gctagatgcc tcctgtatta aaattgagcg tgtgattggt 1920
gcaggagaat tcggtgaagt ctgcagtggc cgtttgaaac ttccagggaa aagagatgtt 1980
gcagtagcca taaaaaccct gaaagttggt tacacagaaa aacaaaggag agacttttttg 2040
tgtgaagcaa gcatcatggg gcagtttgac cacccaaatg ttgtccattt ggaaggggtt 2100
gttacaagag ggaaaccagt catgatagta atagagttca tggaaaatgg agccctagat 2160
gcatttctca ggaaacatga tgggcaattt acagtcattc agttagtagg aatgctgaga 2220
ggaattgctg ctggaatgag atatttggct gatatgggat atgttcacag ggaccttgca 2280
gctcgcaata ttcttgtcaa cagcaatctc gtttgtaaag tgtcagattt tggcctgtcc 2340
cgagttatag aggatgatcc agaagctgtc tatacaacta ctggtggaaa aattccagta 2400
aggtggacag cacccgaagc catccagtac cggaaattca catcagccag tgatgtatgg 2460
agctatggaa tagtcatgtg ggaagttatg tcttatggag aaagaccttа ttgggacatg 2520
tcaaatcaag atgttataaa agcaatagaa gaaggttatc gtttaccagc acccatggac 2580
tgcccagctg gccttcacca gctaatgttg gattgttggc aaaaggagcg tgctgaaagg 2640
ccaaaatttg aacagatagt tggaattcta gacaaaatga ttcgaaaccc aaatagtctg 2700
aaaactcccc tgggaacttg tagtaggcca ataagccctc ttctggatca aaacactcct 2760
gatttcacta ccttttgttc agttggagaa tggctacaag ctattaagat ggaaagatat 2820
aaagataatt tcacggcagc tggctacaat tcccttgaat cagtagccag gatgactatt 2880
gaggatgtga tgagtttagg gatcacactg gttggtcatc aaaagaaaat catgagcagc 2940
attcagacta tgagagcaca aatgctacat ttacatggaa ctggcattca agtgtga 2997

<210> 6
<211> 3217
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin A8
<310> XM001921

<400> 6
ncbsncvwrb mdnctdrtng nmstrctrst tanmymmsar chbmdrtnnc tdstrctrgn 60
mstmmtanmy rmtsndhstr ycbardasna stagnbankg rahcsmdatv washtmantt 120
hdbrandnkb arggnbankh msanshahar tntanmycsm bmrnarnvdn tnhmsansha 180
hamrnaaccs snmvrsnmga tggcccccgc ccggggccgc ctgccccctg cgctctgggt 240
cgtcacggcc gcggcggcgg cggccacctg cgtgtccgcg gcgcgcggcg aagtgaattt 300
gctggacacg tcgaccatcc acggggactg gggctggctc acgtatccgg ctcatgggtg 360
ggactccatc aacgaggtgg acgagtcctt ccagcccatc cacacgtacc aggtttgcaa 420
cgtcatgagc cccaaccaga acaactggct gcgcacgagc tgggtccccc gagacggcgc 480
ccggcgcgtc tatgctgaga tcaagtttac cctgcgcgac tgcaacagca tgcctggtgt 540
gctgggcacc tgcaaggaga ccttcaacct ctactacctg gagtcggacc gcgacctggg 600
ggccagcaca caagaaagcc agttcctcaa aatcgacacc attgcggccg acgagagctt 660
cacaggtgcc gaccttggtg tgcggcgtct caagctcaac acggaggtgc gcagtgtggg 720
tcccctcagc aagcgcggct tctacctggc cttccaggac ataggtgcct gcctggccat 780
cctctctctc cgcatctact ataagaagtg ccctgccatg gtgcgcaatc tggctgcctt 840
ctcggaggca gtgacggggg ccgactcgtc ctcactggtg gaggtgaggg gccagtgcgt 900
gcggcactca gaggagcggg acacacccaa gatgtactgc agcgcggagg gcgagtggct 960
cgtgcccatc ggcaaatgcg tgtgcagtgc cggctacgag gagcggcggg atgcctgtgt 1020
ggcctgtgag ctgggcttct acaagtcagc ccctggggac cagctgtgtg cccgctgccc 1080
tccccacagc cactccgcag ctccagccgc ccaagcctgc cactgtgacc tcagctacta 1140
ccgtgcagcc ctggacccgc cgtctccagc ctgcacccgg ccaccctccg caccagtgaa 1200
cctgatctcc agtgtgaatg ggacatcagt gactctggag tgggcccctc ccctggaccc 1260
aggtggccgc agtgacatca cctacaatgc cgtgtgccgc cgctgcccct gggcactgag 1320

ccgctgcgag gcatgtggga gcggcacccg ctttgtgccc cagcagacaa gcctggtgca 1380
ggccagcctg ctggtggcca acctgctggc ccacatgaac tactccttct ggatcgaggc 1440
cgtcaatggc gtgtccgacc tgagccccga gccccgccgg gccgctgtgg tcaacatcac 1500
cacgaaccag gcagccccgt cccaggtggt ggtgatccgt caagagcggg cgggcagac 1560
cagcgtctcg ctgctgtggc aggagcccga gcagccgaac ggcatcatcc tggagtatga 1620
gatcaagtac tacgagaagg acaaggagat gcagagctac tccaccctca aggccgtcac 1680
caccagagcc accgtctccg gcctcaagcc gggcacccgc tacgtgttcc aggtccgagc 1740
ccgcacctca gcaggctgtg gccgcttcag caggccatg gaggtggaga ccgggaaacc 1800
ccggccccgc tatgacacca ggaccattgt ctggatctgc ctgacgctca tcacgggcct 1860
ggtggtgctt ctgctcctgc tcatctgcaa gaagaggcac tgtggctaca gcaaggactt 1920
ccaggactcg gacgaggaga agatgcacta tcagaatgga caggcacccc cacctgtctt 1980
cctgcctctg catcacccca cgggaaagct cccagagccc cagttctatg cggaacccca 2040
cacctacgag gagccaggcc gggcgggccg cagtttcact cgggagatcg aggcctctag 2100
gatcccacatc gagaaaatca tcggctctgg agactccggg gaagtctgct acgggaggct 2160
gcgggtgcca gggcagcggg atgtgcccgt ggccatcaag gccctcaaag ccggctacac 2220
ggagagacag aggcgggact tcctgagcga ggcgtccatc atgggcaat tcgaccatcc 2280
caacatcatc cgcctcgagg gtgtcgtcac ccgtggccgc ctggcaatga ttgtgactga 2340
gtacatggag aacggctctc tggacacctt cctgaggacc cacgacgggc agttcaccat 2400
catgcagctg gtgggcatgc tgagaggagt gggtgccggc atgcgctacc tctcagacct 2460
gggctatgtc caccgagacc tggccgcccg caacgtcctg gttgacagca acctggtctg 2520
caaggtgtct gacttcgggc tctcacgggt gctggaggac gacccggatg ctgcctacac 2580
caccacgggc gggaagatcc ccatccgctg gacggcccca gaggccatcg ccttccgcac 2640
cttctcctcg gccagcgacg tgtggagctt cggcgtggtc atgtgggagg tgctggccta 2700
tggggagcgg cctactgga acatgaccaa ccgggatgtc atcagctctg tggaggaggg 2760
gtaccgcctg cccgcaccca tgggctgccc ccacgccctg caccagctca tgctcgactg 2820
ttggcacaag gaccgggcgc agcggcctcg cttctcccag attgtcagtg tcctcgatgc 2880
gctcatccgc agccctgaga gtctcagggc caccgccaca gtcagcaggt gcccaccccc 2940
tgccttcgtc cggagctgct ttgacctccg aggggcagc ggtggcggtg gcggcctcac 3000
cgtgggggac tggctggact ccatccgcat gggccggtac cgagaccact tcgctgcggg 3060
cggatactcc tcttcgggca tggtgctacg catgaacgcc caggacgtgc gcgcctgggg 3120
catcaccctc atgggccacc agaagaagat cctgggcagc attcagacca tgcgggccca 3180
gctgaccagc acccaggggc cccgccggca cctctga 3217

<210> 7
<211> 1497
<212> DNA
<213> Homo sapiens

<300>
<308> U83508

<300>
<302> angiopoietin 2
<310> U83508

<400> 7
atgacagttt tcctttcctt tgctttcctc gctgccattc tgactcacat agggtgcagc 60
aatcagcgcc gaagtccaga aaacagtggg agaagatata accggattca acatgggcaa 120
tgtgcctaca ctttcattct tccagaacac gatggcaact gtcgtgagag tacgacagac 180
cagtacaaca caaacgctct gcagagagat gctccacacg tggaaccgga tttctcttcc 240
cagaaacttc aacatctgga acatgtgatg gaaaattata ctcagtggct gcaaaaactt 300
gagaattaca ttgtggaaaa catgaagtcg gagatggccc agatacagca gaatgcagtt 360
cagaaccaca cggctaccat gctggagata ggaaccagcc tcctctctca gactgcagag 420
cagaccagaa agctgacaga tgttgagacc caggtactaa atcaaacttc tcgacttgag 480
atacagctgc tggagaattc attatccacc tacaagctag agaagcaact tcttcaacag 540
acaaatgaaa tcttgaagat ccatgaaaaa aacagtttat tagaacataa aatcttagaa 600
atggaaggaa aacacaagga agagttggac accttaaagg aagagaaaga gaaccttcaa 660
ggcttggtta ctcgtcaaac atatataatc caggagctgg aaaagcaatt aaacagagct 720
accaccaaca acagtgtcct tcagaagcag caactggagc tgatggacac agtccacaac 780

```
cttgtcaatc tttgcactaa agaaggtgtt ttactaaagg gaggaaaaag agaggaagag 840
aaaccatttta gagactgtgc agatgtatat caagctggtt ttaataaaag tggaatctac 900
actatttata ttaataatat gccagaaccc aaaaaggtgt tttgcaatat ggatgtcaat 960
gggggaggtt ggactgtaat acaacatcgt gaagatggaa gtctagattt ccaaagaggc 1020
tggaaggaat ataaaatggg ttttggaaat ccctccggtg aatattggct ggggaatgag 1080
tttatttttg ccattaccag tcagaggcag tacatgctaa gaattgagtt aatggactgg 1140
gaagggaacc gagcctattc acagtatgac agattccaca taggaaatga aaagcaaaac 1200
tataggttgt atttaaaagg tcacactggg acagcaggaa aacagagcag cctgatctta 1260
cacggtgctg atttcagcac taaagatgct gataatgaca actgtatgtg caaatgtgcc 1320
ctcatgttaa caggaggatg gtggtttgat gcttgtggcc cctccaatct aaatggaatg 1380
ttctatactg cgggacaaaa ccatggaaaa ctgaatggga taaagtggca ctacttcaaa 1440
gggcccagtt actccttacg ttccacaact atgatgattc gacctttaga tttttga    1497
```

<210> 8
<211> 3417
<212> DNA
<213> Homo sapiens

<300>
<310> XM001924

<300>
<302> Tie1

<400> 8

```
atggtctggc gggtgccccc tttcttgctc cccatcctct tcttggcttc tcatgtgggc 60
gcggcggtgg acctgacgct gctggccaac ctgcggctca cggaccccca gcgcttcttc 120
ctgacttgcg tgtctgggga ggccggggcg gggaggggct cggacgcctg gggcccgccc 180
ctgctgctgg agaaggacga ccgtatcgtg cgcaccccgc ccgggccacc cctgcgcctg 240
gcgcgcaacg gttcgcacca ggtcacgctt cgcggcttct ccaagccctc ggacctcgtg 300
ggcgtcttct cctgcgtggg cggtgctggg gcgcggcgca cgcggctcat ctacgtgcac 360
aacagccctg gagccccact gcttccagac aaggtcacac acactgtgaa caaaggtgac 420
accgctgtac tttctgcacg tgtgcacaag gagaagcaga cagacgtgat ctggaagagc 480
aacggatcct acttctacac cctggactgg catgaagccc aggatgggcg gttcctgctg 540
cagctcccaa atgtgcagcc accatcgagc ggcatctaca gtgccactta cctggaagcc 600
agccccctgg gcagcgcctt ctttcggctc atcgtgcggg gttgtggggc tgggcgctgg 660
gggccaggct gtaccaagga gtgcccaggt tgcctacatg gaggtgtctg ccacgaccat 720
gacggcgaat gtgtatgccc ccctggcttc actggcaccc gctgtgaaca ggcctgcaga 780
gagggccgtt ttgggcagag ctgccaggag cagtgcccag gcatatcagg ctgccggggc 840
ctcacctttct gcctcccaga ccccatggc tgctcttgtg gatctggctg gagaggaagc 900
cagtgccaag aagcttgtgc ccctggtcat tttgggggctg attgccgact ccagtgccag 960
tgtcagaatg gtggcacttg tgaccggttc agtgttgtg tctgcccctc tgggtggcat 1020
ggagtgcact gtgagaagtc agaccggatc ccccagatcc tcaacatggc ctcagaactg 1080
gagttcaact tagagacgat gccccggatc aactgtgcag ctgcagggaa ccccttcccc 1140
gtgcgggcga gcatagagct acgcaagcca gacggcactg tgctcctgtc caccaaggcc 1200
attgtggagc cagagaagac cacagctgag ttcgaggtgc cccgcttggt tcttgcggac 1260
agtgggttct gggagtgccg tgtgtccaca tctggcggcc aagacagccg gcgcttcaag 1320
gtcaatgtga aagtgccccc cgtgcccctg gctgcacctc ggctcctgac caagcagagc 1380
cgccagcttg tggtctcccc gctggtctcg ttctctgggg atggacccat ctccactgtc 1440
cgcctgcact accggcccca ggacagtacc atggactggt cgaccattgt ggtggacccc 1500
agtgagaacg tgacgttaat gaacctgagg ccaaagacag gatacagtgt tcgtgtgcag 1560
ctgagccggc caggggaagg aggagagggg gcctgggggc ctcccacctt catgaccaca 1620
gactgtcctg agccttgttt gcagccgtgg ttggaggtct ggcatgtgga aggcactgac 1680
cggctgcgag tgagctggtc cttgcccttg gtgcccgggc cactggtggg cgacggtttc 1740
ctgctgcgcc tgtgggacgg gacacggggg caggagcggc gggagaacgt ctcatccccc 1800
caggcccgca ctgccctcct gacgggactc acgcctggca cccactacca gctggatgtg 1860
cagctctacc actgcaccct cctgggcccg gcctcgcccc ctgcacacgt gcttctgccc 1920
ccagtgggc ctccagcccc ccgacacctc cacgcccagg ccctctcaga ctccgagatc 1980
cagctgacat ggaagcaccc ggaggctctg cctgggccaa tatccaagta cgttgtggag 2040
```

gtgcaggtgg ctgggggtgc aggagaccca ctgtggatag acgtggacag gcctgaggag 2100
acaagcacca tcatccgtgg cctcaacgcc agcacggcct acctcttccg catgcgggcc 2160
agcattcagg ggctcgggga ctggagcaac acagtagaag agtccaccct gggcaacggg 2220
ctgcaggctg aggcccagtc ccaagagagc cgggcagctg aagagggcct ggatcagcag 2280
ctgatcctgg cggtggtggg ctccgtgtct gccacctgcc tcaccatcct ggctgccctt 2340
ttaaccctgg tgtgcatccg cagaagctgc ctgcatcgga gacgcacctt cacctaccag 2400
tcaggctccg gcgaggagac catcctgcag ttcagctcag ggacctttgac acttacccgg 2460
cggccaaaac tgcagcccga gcccctgagc tacccagtgc tagagtggga tgacatcacc 2520
tttgaggacc tcatcgggga ggggaacttc ggccaggtca tccgggccat gatcaagaag 2580
gacgggctga agatgaacgc agccatcaaa atgctgaaag agtatgcctc tgaaaatgac 2640
catcgtgact ttgcgggaga actggaagtt ctgtgcaaat tggggcatca ccccaacatc 2700
atcaacctcc tgggggcctg taagaaccga ggttacttgt atatcgctat tgaatatgcc 2760
ccctacggga acctgctaga tttttctgcg aaaagccggg tcctagagac tgacccagct 2820
tttgctcgag agcatgggac agcctctacc tttagctccc ggcagctgct gcgtttcgcc 2880
agtgatgcgg ccaatggcat gcagtacctg agtgagaagc agttcatcca cagggacctg 2940
gctgcccgga atgtgctggt cggagagaac ctggcctcca agattgcaga cttcggcctt 3000
tctcggggag aggaggttta tgtgaagaag acgatggggc gtctccctgt gcgctggatg 3060
gccattgagt ccctgaacta cagtgtctat accaccaaga gtgatgtctg gtcctttgga 3120
gtcttcttt gggagatagt gagccttgga ggtacaccct actgtggcat gacctgtgcc 3180
gagctctatg aaaagctgcc ccagggctac cgcatggagc agcctcgaaa ctgtgacgat 3240
gaagtgtacg agctgatgcg tcagtgctgg cgggaccgtc cctatgagcg accccccttt 3300
gcccagattg cgctacagct aggccgcatg ctggaagcca ggaaggccta tgtgaacatg 3360
tcgctgtttg agaacttcac ttacgcgggc attgatgcca cagctgagga ggcctga 3417

<210> 9
<211> 3375
<212> DNA
<213> Homo sapiens

<300>
<302> TEK
<310> L06139

<400> 9
atggactctt tagccagctt agttctctgt ggagtcagct tgctcctttc tggaactgtg 60
gaaggtgcca tggacttgat cttgatcaat tccctacctc ttgtatctga tgctgaaaca 120
tctctcacct gcattgcctc tgggtggcgc ccccatgagc ccatcaccat aggaagggac 180
tttgaagcct taatgaacca gcaccaggat ccgctggaag ttactcaaga tgtgaccaga 240
gaatgggcta aaaaagttgt ttggaagaga gaaaaggcta gtaagatcaa tggtgcttat 300
ttctgtgaag ggcgagttcg aggaggagca atcaggatac gaaccatgaa gatgcgtcaa 360
caagcttcct tcctaccagc tactttaact atgactgtgg acaagggaga taacgtgaac 420
atatctttca aaaaggtatt gattaaagaa gaagatgcag tgatttacaa aaatggttcc 480
ttcatccatt cagtgcccca gcatgaagta cctgatattc tagaagtaca cctgcctcat 540
gctcagcccc aggatgctgg agtgtactcg gccaggtata taggaggaaa cctctttcacc 600
tcggccttca ccaggctgat agtccggaga tgtgaagccc agaagtgggg acctgaatgc 660
aaccatctct gtactgcttg tatgaacaat ggtgtctgcc atgaagatac tggagaatgc 720
atttgccctc ctgggtttat gggaaggacg tgtgagaagg cttgtgaact gcacacgttt 780
ggcagaactt gtaaagaaag gtgcagtgga caagaggat gcaagtctta tgtgttctgt 840
ctccctgacc cctatgggtg ttcctgtgcc acaggctgga agggtctgca gtgcaatgaa 900
gcatgccacc ctggttttta cgggccagat tgtaagctta ggtgcagctg caacaatggg 960
gagatgtgtg atcgcttcca aggatgtctc tgctctccag gatggcaggg gctccagtgt 1020
gagagagaag gcataccgag gatgacccca aagatagtgg atttgccaga tcatatagaa 1080
gtaaacagtg gtaaatttaa tcccatttgc aaagcttctg gctggccgct acctactaat 1140
gaagaaatga ccctggtgaa gccggatggg acagtgctcc atccaaaaga ctttaaccat 1200
acggatcatt tctcagtagc catattcacc atccaccgga tcctcccccc tgactcagga 1260
gtttgggtct gcagtgtgaa cacagtggct gggatggtgg aaaagccctt caacatttct 1320
gttaaagttc ttccaaagcc cctgaatgcc ccaaacgtga ttgacactgg acataacttt 1380
gctgtcatca acatcagctc tgagccttac tttggggatg gaccaatcaa atccaagaag 1440
cttctataca aacccgttaa tcactatgag gcttggcaac atattcaagt gacaaatgag 1500

attgttacac tcaactattt ggaacctcgg acagaatatg aactctgtgt gcaactggtc 1560
cgtcgtggag agggtgggga agggcatcct ggacctgtga gacgcttcac aacagcttct 1620
atcggactcc ctcctccaag aggtctaaat ctcctgccta aaagtcagac cactctaaat 1680
ttgacctggc aaccaatatt tccaagctcg gaagatgact tttatgttga agtggagaga 1740
aggtctgtgc aaaaaagtga tcagcagaat attaaagttc caggcaactt gacttcggtg 1800
ctacttaaca acttacatcc cagggagcag tacgtggtcc gagctagagt caacaccaag 1860
gcccaggggg aatggagtga agatctcact gcttggaccc ttagtgacat tcttcctcct 1920
caaccagaaa acatcaagat ttccaacatt acacactcct cggctgtgat ttcttggaca 1980
atattggatg gctattctat ttcttctatt actatccgtt acaaggttca aggcaagaat 2040
gaagaccagc acgttgatgt gaagataaag aatgccacca tcattcagta tcagccaag 2100
ggcctagagc ctgaaacagc ataccaggtg gacatttttg cagagaacaa catagggtca 2160
agcaacccag ccttttctca tgaactggtg acccctccag aatctcaagc accagcggac 2220
ctcggagggg ggaagatgct gcttatagcc atccttggct ctgctggaat gacctgcctg 2280
actgtgctgt tggcctttct gatcatattg caattgaaga gggcaaatgt gcaaaggaga 2340
atggcccaag ccttccaaaa cgtgaggggaa gaaccagctg tgcagttcaa ctcagggact 2400
ctggccctaa acaggaaggt caaaaacaac ccagatccta caatttatcc agtgcttgac 2460
tggaatgaca tcaaatttca agatgtgatt ggggagggca attttggcca agttcttaag 2520
gcgcgcatca agaaggatgg gttacggatg gatgctgcca tcaaaagaat gaaagaatat 2580
gcctccaaag atgatcacag ggactttgca ggagaactgg aagttctttg taaacttgga 2640
caccatccaa acatcatcaa tctcttagga gcatgtgaac atcgaggcta cttgtacctg 2700
gccattgagt acgcgcccca tggaaacctt ctggacttcc ttcgcaagag ccgtgtgctg 2760
gagacggacc cgacatttgc cattgccaat agcaccgcgt ccacactgtc ctcccagcag 2820
ctccttcact tcgctgccga cgtggcccgg ggcatggact acttgagcca aaaacagttt 2880
atccacaggg atctggctgc cagaaacatt ttagttggtg aaaactatgt ggcaaaaata 2940
gcagattttg gattgtcccg aggtcaagag gtgtacgtga aaaagacaat gggaaggctc 3000
ccagtgcgct ggatggccat cgagtcactg aattacagtg tgtacacaac caacagtgat 3060
gtatggtcct atggtgtgtt actatgggag attgttagct taggaggcac accctactgc 3120
gggatgactt gtgcagaact ctacgagaag ctgccccagg gctacagact ggagaagccc 3180
ctgaactgtg atgatgaggt gtatgatcta atgagacaat gctggcggga gaagccttat 3240
gagaggccat catttgccca gatattggtg tccttaaaca gaatgttaga ggagcgaaag 3300
acctacgtga ataccacgct ttatgagaag tttacttatg caggaattga ctgttctgct 3360
gaagaagcgg cctag 3375

<210> 10
<211> 2409
<212> DNA
<213> Homo sapiens

<300>

<300>
<302> beta5 integrin
<310> X53002

<400> 10
ncbsncvwra tgccgcgggc cccggcgccg ctgtacgcct gcctcctggg gctctgcgcg 60
ctcctgcccc ggctcgcagg tctcaacata tgcactagtg gaagtgccac ctcatgtgaa 120
gaatgtctgc taatccaccc aaaatgtgcc tggtgctcca aagaggactt cggaagccca 180
cggtccatca cctctcggtg tgatctgagg gcaaaccttg tcaaaaatgg ctgtggaggt 240
gagatagaga gcccagccag cagcttccat gtcctgagga gcctgcccct cagcagcaag 300
ggttcgggct ctgcaggctg ggacgtcatt cagatgacac cacaggagat tgccgtgaac 360
ctccggcccg gtgacaagac caccttccag ctacaggttc gccaggtgga ggactatcct 420
gtggacctgt atcacctgat ggacctctcc ctgtccatga aggatgactt ggacaatatc 480
cggagcctgg gcaccaaact cgcggaggag atgaggaagc tcaccagcaa cttccggttg 540
ggatttgggt cttttgttga taaggacatc tctcctttct cctacacggc accgaggtac 600
cagaccaatc cgtgcattgg ttacaagttg tttccaaatt gcgtcccctc ctttgggttc 660
cgccatctgc tgcctctcac agacagagtg gacagcttca atgaggaagt tcggaaacag 720
agggtgtccc ggaaccgaga tgcccctgag gggggctttg atgcagtact ccaggcagcc 780
gtctgcaagg agaagattgg ctggcgaaag gatgcactgc atttgctggt gttccacaaca 840

gatgatgtgc cccacatcgc attggatgga aaattgggag gcctggtgca gccacacgat 900
ggccagtgcc acctgaacga ggccaacgag tacacagcat ccaaccagat ggactatcca 960
tcccttgcct tgcttggaga gaaattggca gagaacaaca tcaacctcat ctttgcagtg 1020
acaaaaaacc attatatgct gtacaagaat tttacagccc tgatacctgg aacaacggtg 1080
gagatttttag atggagactc caaaaatatt attcaactga ttattaatgc atacaatagt 1140
atccggtcta aagtggagtt gtcagtctgg gatcagcctg aggatcttaa tctcttcttt 1200
actgctacct gccaagatgg ggtatcctat cctggtcaga ggaagtgtga gggtctgaag 1260
attgggaca cggcatcttt tgaagtatca ttggaggccc gaagctgtcc cagcagacac 1320
acggagcatg tgtttgccct gcggccggtg ggattccggg acagcctgga ggtgggggtc 1380
acctacaact ccagctgcgg ctgcagcgtg gggctggaac ccaacagcgc caggtgcaac 1440
gggagcggga cctatgtctg cggcctgtgt gagtgcagcc ccggctacct gggcaccagg 1500
tgcgagtgcc aggatgggga gaaccagagc gtgtaccaga acctgtgccg ggaggcagag 1560
ggcaagccac tgtgcagcgg gcgtggggac tgcagctgca accagtgctc ctgcttcgag 1620
agcgagtttg gcaagatcta tgggcctttc tgtgagtgcg acaacttctc ctgtgccagg 1680
aacaagggag tcctctgctc aggccatggc gagtgtcact gcgggaatg caagtgccat 1740
gcaggttaca tcggggacaa ctgtaactgc tcgacagaca tcagcacatg ccggggcaga 1800
gatggccaga tctgcagcga gcgtgggcac tgtctctgtg ggcagtgcca atgcacggag 1860
ccgggggcct ttggggagat gtgtgagaag tgccccacct gcccggatgc atgcagcacc 1920
aagagagatt gcgtcgagtg cctgctgctc cactctggga aacctgacaa ccagacctgc 1980
cacagcctat gcagggatga ggtgatcaca tgggtggaca ccatcgtgaa agatgaccag 2040
gaggctgtgc tatgtttcta caaaaccgcc aaggactgcg tcatgatgtt cacctatgtg 2100
gagctcccca gtgggaagtc caacctgacc gtcctcaggg agccagagtg tggaaacacc 2160
cccaacgcca tgaccatcct cctggctgtg gtcggtagca tcctccttgt tgggcttgca 2220
ctcctggcta tctggaagct gcttgtcacc attcacgacc ggagggagtt tgcaaagttt 2280
cagagcgagc gatccagggc ccgctatgaa atggcttcaa atccattata cagaaagcct 2340
atctccacgc acactgtgga cttcaccttc aacaagttca acaaatccta caatggcact 2400
gtggactga 2409

<210> 11
<211> 2367
<212> DNA
<213> Homo sapiens

<300>
<302> beta3 integrin
<310> NM000212

<400> 11
atgcgagcgc ggccgcggcc ccggccgctc tgggcgactg tgctggcgct gggggcgctg 60
gcgggcgttg gcgtaggagg gcccaacatc tgtaccacgc gaggtgtgag ctcctgccag 120
cagtgcctgg ctgtgagccc catgtgtgcc tggtgctctg atgaggccct gcctctgggc 180
tcacctcgct gtgacctgaa ggagaatctg ctgaaggata actgtgcccc agaatccatc 240
gagttcccag tgagtgaggc ccgagtacta gaggacaggc ccctcagcga caaggctct 300
ggagacagct cccaggtcac tcaagtcagt ccccagagga ttgcactccg gctccggcca 360
gatgattcga agaatttctc catccaagtg cggcaggtgg aggattaccc tgtggacatc 420
tactacttga tggacctgtc ttactccatg aaggatgatc tgtggagcat ccagaacctg 480
ggtaccaagc tggccaccca gatgcgaaag ctcaccagta acctgcggat tggcttcggg 540
gcatttgtgg acaagcctgt gtcaccatac atgtatatct ccccaccaga ggccctcgaa 600
aaccccgct atgatatgaa gaccacctgc ttgcccatgt ttggctacaa acacgtgctg 660
acgctaactg accaggtgac ccgcttcaat gaggaagtga agaagcagag tgtgtcacgg 720
aaccgagatg ccccagaggg tggctttgat gccatcatgc aggctacagt ctgtgatgaa 780
aagattggct ggaggaatga tgcatcccac ttgctggtgt ttaccactga tgccaagact 840
catatagcat tggacggaag gctggcaggc attgtccagc ctaatgacgg gcagtgtcat 900
gttggtagtg acaatcatta ctctgcctcc actaccatgg attatccctc tttgggggctg 960
atgactgaga agctatccca gaaaaacatc aatttgatct ttgcagtgac tgaaaatgta 1020
gtcaatctct atcagaacta tagtgagctc atcccaggga ccacagttgg ggttctgtcc 1080
atggattcca gcaatgtcct ccagctcatt gttgatgctt atgggaaaat ccgttctaaa 1140
gtagagctgg aagtgcgtga cctccctgaa gagttgtctc tatccttcaa tgccacctgc 1200
ctcaacaatg aggtcatccc tggcctcaag tcttgtatgg gactcaagat tggagacacg 1260

gtgagcttca gcattgaggc caaggtgcga ggctgtcccc aggagaagga gaagtccttt 1320
accataaagc ccgtgggctt caaggacagc ctgatcgtcc aggtcacctt tgattgtgac 1380
tgtgcctgcc aggcccaagc tgaacctaat agccatcgct gcaacaatgg caatgggacc 1440
tttgagtgtg gggtatgccg ttgtgggcct ggctggctgg gatcccagtg tgagtgctca 1500
gaggaggact atcgcccttc ccagcaggac gaatgcagcc cccgggaggg tcagcccgtc 1560
tgcagccagc gggqcgagtg cctctgtggt caatgtgtct gccacagcag tgactttggc 1620
aagatcacgg gcaagtactg cgagtgtgac gacttctcct gtgtccgcta caagggggag 1680
atgtgctcag gccatggcca gtgcagctgt ggggactgcc tgtgtgactc cgactggacc 1740
ggctactact gcaactgtac cacgcgtact gacacctgca tgtccagcaa tgggctgctg 1800
tgcagcggcc gcggcaagtg tgaatgtggc agctgtgtct gtatccagcc gggctcctat 1860
ggggacacct gtgagaagtg ccccacctgc ccagatgcct gcacctttaa gaaagaatgt 1920
gtggagtgta agaagtttga ccgggagccc tacatgaccg aaaatacctg caaccgttac 1980
tgccgtgacg agattgagtc agtgaaagag cttaaggaca ctggcaagga tgcagtgaat 2040
tgtacctata agaatgagga tgactgtgtc gtcagattcc agtactatga agatttctagt 2100
ggaaagtcca tcctgtatgt ggtagaagag ccagagtgtc ccaagggccc tgacatcctg 2160
gtggtcctgc tctcagtgat gggggccatt ctgctcattg gccttgccgc ctgctcatc 2220
tggaaactcc tcatcaccat ccacgaccga aaagaattcg ctaaatttga ggaagaacgc 2280
gccagagcaa aatgggacac agccaacaac ccactgtata aagaggccac gtctaccttc 2340
accaatatca cgtaccgggg cacttaa 2367

<210> 12
<211> 3147
<212> DNA
<213> Homo sapiens

<300>
<302> alpha v intergrin
<310> NM0022210

<400> 12
atggcttttc cgccgcggcg acggctgcgc ctcggtcccc gcggcctccc gcttcttctc 60
tcgggactcc tgctacctct gtgccgcgcc ttcaacctag acgtggacag tcctgccgag 120
tactctggcc ccgagggaag ttacttcggc ttcgccgtgg atttcttcgt gcccagcgcg 180
tcttcccgga tgtttcttct cgtgggagct cccaaagcaa acaccaccca gcctgggatt 240
gtggaaggag ggcaggtcct caaatgtgac tggtcttcta cccgccggtg ccagccaatt 300
gaatttgatg caacaggcaa tagagattat gccaaggatg atccattgga atttaagtcc 360
catcagtggt ttggagcatc tgtgaggtcg aaacaggata aaattttggc ctgtgcccca 420
ttgtaccatt ggagaactga gatgaaacag gagcgagagc ctgttggaac atgctttctt 480
caagatggaa caaagactgt tgagtatgct ccatgtagat cacaagatat tgatgctgat 540
ggacagggat tttgtcaagg aggattcagc attgatttta ctaaagctga cagagtactt 600
cttggtggtc ctggtagctt ttattggcaa ggtcagctta tttcggatca agtggcagaa 660
atcgtatcta aatacgaccc caatgtttac agcatcaagt ataataacca attagcaact 720
cggactgcac aagctatttt tgatgacagc tatttgggtt attctgtggc tgtcggagat 780
ttcaatggtg atggcataga tgacttttgt tcaggagttc caagagcagc aaggactttg 840
ggaatggttt atatttatga tgggaagaac atgtcctcct tatacaattt tactggcgag 900
cagatggctg catatttcgg attttctgta gctgccactg acattaatgg agatgattat 960
gcagatgtgt ttattggagc acctctcttc atggatcgtg gctctgatgg caaactccaa 1020
gaggtggggc aggtctcagt gtctctacag agagctttcag gagacttcca gacgacaaag 1080
ctgaatggat ttgaggtctt tgcacggttt ggcagtgcca tagctccttt gggagatctg 1140
gaccaggatg gtttcaatga tattgcaatt gctgctccat atgggggtga agataaaaaa 1200
ggaattgttt atatcttcaa tggaagatca acaggcttga acgcagtccc atctcaaatc 1260
cttgaagggc agtgggctgc tcgaagcatg ccaccaagct ttggctattc aatgaaagga 1320
gccacagata tagacaaaaa tggatatcca gacttaattg taggagcttt tggtgtagat 1380
cgagctatct tatacagggc cagaccagtt atcactgtaa atgctggtct tgaagtgtac 1440
cctagcattt taaatcaaga caataaaacc tgctcactgc ctggaacagc tctcaaagtt 1500
tcctgtttta atgttaggtt ctgcttaaag gcagatggca aaggagtact tcccaggaaa 1560
cttaatttcc aggtggaact tcttttggat aaactcaagc aaaagggagc aattcgacga 1620
gcactgtttc tctacagcag gtccccaagt cactccaaga acatgactat ttcaaggggg 1680
ggactgatgc agtgtgagga attgatagcg tatctgcggg atgaatctga atttagagac 1740

aaactcactc caattactat ttttatggaa tatcggttgg attatagaac agctgctgat 1800
acaacaggct tgcaacccat tcttaaccag ttcacgcctg ctaacattag tcgacaggct 1860
cacattctac ttgactgtgg tgaagacaat gtctgtaaac ccaagctgga agtttctgta 1920
gatagtgatc aaaagaagat ctatattggg gatgacaacc ctctgacatt gattgttaag 1980
gctcagaatc aaggagaagg tgcctacgaa gctgagctca tcgtttccat tccactgcag 2040
gctgatttca tcggggttgt ccgaaacaat gaagccttag caagactttc ctgtgcattt 2100
aagacagaaa accaaactcg ccaggtggta tgtgaccttg gaaacccaat gaaggctgga 2160
actcaactct tagctggtct tcgtttcagt gtgcaccagc agtcagagat ggatacttct 2220
gtgaaatttg acttacaaat ccaaagctca aatctatttg acaaagtaag cccagttgta 2280
tctcacaaag ttgatcttgc tgttttagct gcagttgaga taagaggagt ctcgagtcct 2340
gatcatatct ttcttccgat tccaaactgg gagcacaagg agaaccctga gactgaagaa 2400
gatgttgggc cagttgttca gcacatctat gagctgagaa acaatggtcc aagttcattc 2460
agcaaggcaa tgctccatct tcagtggcct tacaaatata ataataacac tctgttgtat 2520
atccttcatt atgatattga tggaccaatg aactgcactt cagatatgga gatcaaccct 2580
ttgagaatta agatctcatc tttgcaaaca actgaaaaga atgacacggt tgccgggcaa 2640
ggtgagcggg accatctcat cactaagcgg gatcttgccc tcagtgaagg agatattcac 2700
actttgggtt gtggagttgc tcagtgcttg aagattgtct gccaagttgg gagattagac 2760
agaggaaaga gtgcaatctt gtacgtaaag tcattactgt ggactgagac ttttatgaat 2820
aaagaaaatc agaatcattc ctatttctctg aagtcgtctg cttcatttaa tgtcatagag 2880
tttccttata agaatctttcc aattgaggat atcaccaact ccacattggt taccactaat 2940
gtcaccctggg gcattcagcc agcgcccatg cctgtgcctg tgtgggtgat cattttagca 3000
gttctagcag gattgttgct actggctgtt ttggtatttg taatgtacag gatgggcttt 3060
tttaaacggg tccggccacc tcaagaagaa caagaaaggg agcagcttca acctcatgaa 3120
aatggtgaag gaaactcaga aacttaa 3147

<210> 13
<211> 402
<212> DNA
<213> Homo sapiens

<300>
<302> CaSm (cancer associated SM-like oncogene)
<310> AF000177

<400> 13
atgaactata tgcctggcac cgccagcctc atcgaggaca ttgacaaaaa gcacttggtt 60
ctgcttcgag atggaaggac acttataggc tttttaagaa gcattgatca atttgcaaac 120
ttagtgctac atcagactgt ggagcgtatt catgtgggca aaaaatacgg tgatattcct 180
cgagggattt ttgtggtcag aggagaaaat gtggtcctac taggagaaat agacttggaa 240
aaggagagtg acacacccct ccagcaagta tccattgaag aaattctaga agaacaaagg 300
gtggaacagc agaccaagct ggaagcagag aagttgaaag tgcaggccct gaaggaccga 360
ggtctttcca ttcctcgagc agatactctt gatgagtact aa 402

<210> 14
<211> 1923
<212> DNA
<213> Homo sapiens

<300>
<302> c-myb
<310> NM005375

<400> 14
atggcccgaa gaccccggca cagcatatat agcagtgacg aggatgatga ggactttgag 60
atgtgtgacc atgactatga tgggctgctt cccaagtctg gaaagcgtca cttggggaaa 120
acaaggtgga cccgggaaga ggatgaaaaa ctgaagaagc tggtggaaca gaatggaaca 180
gatgactgga aagttattgc caattatctc ccgaatcgaa cagatgtgca gtgccagcac 240
cgatggcaga aagtactaaa ccctgagctc atcaagggtc cttggaccaa agaagaagat 300

cagagagtga tagagcttgt acagaaatac ggtccgaaac gttggtctgt tattgccaag 360
cacttaaagg ggagaattgg aaaacaatgt agggagaggt ggcataacca cttgaatcca 420
gaagttaaga aaacctcctg gacagaagag gaagacagaa ttatttacca ggcacacaag 480
agactgggga acagatgggc agaaatcgca aagctactgc ctggacgaac tgataatgct 540
atcaagaacc actggaattc tacaatgcgt cggaaggtcg aacaggaagg ttatctgcag 600
gagtcttcaa aagccagcca gccagcagtg gccacaagct tccagaagaa cagtcatttg 660
atgggttttg ctcaggctcc gcctacagct caactccctg ccactggcca gcccactgtt 720
aacaacgact attcctatta ccacatttct gaagcacaaa atgtctccag tcatgttcca 780
taccctgtag cgttacatgt aaatatagtc aatgtccctc agccagctgc cgcagccatt 840
cagagacact ataatgatga agaccctgag aaggaaaagc gaataaagga attagaattg 900
ctcctaatgt caaccgagaa tgagctaaaa ggacagcagg tgctaccaac acagaaccac 960
acatgcagct accccgggtg gcacagcacc accattgccg accacaccag acctcatgga 1020
gacagtgcac ctgtttcctg tttgggagaa caccactcca ctccatctct gccagcggat 1080
cctggctccc tacctgaaga aagcgcctcg ccagcaaggt gcatgatcgt ccaccagggc 1140
accattctgg ataatgttaa gaacctctta gaatttgcag aaacactcca atttatagat 1200
tctttcttaa acacttccag taaccatgaa aactcagact tggaaatgcc ttctttaact 1260
tccacccccc tcattggtca caaattgact gttacaacac catttcatag agaccagact 1320
gtgaaaactc aaaaggaaaa tactgttttt agaaccccag ctatcaaaag gtcaatctta 1380
gaaagctctc caagaactcc tacaccattc aaacatgcac ttgcagctca agaaattaaa 1440
tacggtcccc tgaagatgct acctcagaca ccctctcatc tagtagaaga tctgcaggat 1500
gtgatcaaac aggaatctga tgaatctgga tttgttgctg agtttcaaga aaatggacca 1560
cccttactga agaaaatcaa acaagaggtg gaatctccaa ctgataaatc aggaaacttc 1620
ttctgctcac accactggga aggggacagt ctgaataccc aactgttcac gcagacctcg 1680
cctgtgcgag atgcaccgaa tattcttaca agctccgttt taatggcacc agcatcagaa 1740
gatgaagaca atgttctcaa agcatttaca gtacctaaaa acaggtccct ggcgagcccc 1800
ttgcagcctt gtagcagtac ctgggaacct gcatcctgtg gaaagatgga ggagcagatg 1860
acatcttcca gtcaagctcg taaatacgtg aatgcattct cagcccggac gctggtcatg 1920
tga 1923

<210> 15
<211> 544
<212> DNA
<213> Homo sapiens

<300>
<302> c-myc
<310> J00120

<400> 15
gacccccgag ctgtgctgct cgcggccgcc accgccgggc cccggccgtc cctggctccc 60
ctcctgcctc gagaagggca gggcttctca gaggcttggc gggaaaaaga acggagggag 120
ggatcgcgct gagtataaaa gccggttttc ggggctttat ctaactcgct gtagtaattc 180
cagcgagagg cagagggagc gagcgggcgg ccggctaggg tggaagagcc gggcgagcag 240
agctgcgctg cgggcgtcct gggaagggag atccggagcg aataggggga ttcgcctctg 300
gcccagccct cccgctgatc ccccagccag cggtccgcaa cccttgccgc atccacgaaa 360
ctttgcccat agcagcgggc gggcactttg cactggaact tacaacaccc gagcaaggac 420
gcgactctcc cgacgcgggg aggctattct gcccatttgg ggacacttcc ccgccgctgc 480
caggacccgc ttctctgaaa ggctctcctt gcagctgctt agacgctgga ttttttcggg 540
gtag 544

<210> 16
<211> 618
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin-A1
<310> NM004428

<400> 16
atggagttcc tctgggcccc tctcttgggt ctgtgctgca gtctggccgc tgctgatcgc 60
cacaccgtct tctggaacag ttcaaatccc aagttccgga atgaggacta caccatacat 120
gtgcagctga atgactacgt ggacatcatc tgtccgcact atgaagatca ctctgtggca 180
gacgctgcca tggagcagta catactgtac ctggtggagc atgaggagta ccagctgtgc 240
cagccccagt ccaaggacca agtccgctgg cagtgcaacc ggccccagtgc caagcatggc 300
ccggagaagc tgtctgagaa gttccagcgc ttcacacctt tcaccctggg caaggagttc 360
aaagaaggac acagctacta ctacatctcc aaacccatcc accagcatga agaccgctgc 420
ttgaggttga aggtgactgt cagtggcaaa atcactcaca gtcctcaggc ccatgtcaat 480
ccacaggaga agagacttgc agcagatgac ccagaggtgc gggttctaca tagcatcggt 540
cacagtgctg ccccacgcct cttcccactt gcctggactg tgctgctcct tccacttctg 600
ctgctgcaaa ccccgtga 618

<210> 17
<211> 642
<212> DNA
<213> Homo sapiens

<400> 17
atggcgcccg cgcagcgccc gctgctcccg ctgctgctcc tgctgttacc gctgccgccg 60
ccgcccttcg cgcgcgccga ggacgccgcc cgcgccaact cggaccgcta cgccgtctac 120
tggaaccgca gcaaccccag gttccacgca ggcgcggggg acgacggcgg gggctacacg 180
gtggaggtga gcatcaatga ctacctggac atctactgcc cgcactatgg ggcgccgctg 240
ccgccggccg agcgcatgga gcactacgtg ctgtacatgg tcaacggcga gggccacgcc 300
tcctgcgacc accgccagcg cggcttcaag cgctgggagt gcaaccggcc cgcggcgccc 360
gggggccgc tcaagttctc ggagaagttc cagctcttca cgccctctc cctgggcttc 420
gagttccggc ccggccacga gtattactac atctctgcca cgcctcccaa tgctgtggac 480
cggccctgcc tgcgactgaa ggtgtacgtg cggccgacca acgagaccct gtacgaggct 540
cctgagccca tcttcaccag caataactcg tgtagcagcc cgggcggctg ccgcctcttc 600
ctcagcacca tccccgtgct ctggaccctc ctgggttcct ag 642

<210> 18
<211> 717
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin-A3
<310> XM001787

<400> 18
atggcggcgg ctccgctgct gctgctgctg ctgctcgtgc ccgtgccgct gctgccgctg 60
ctggcccaag ggcccggagg ggcgctggga aaccggcatg cggtgtactg gaacagctcc 120
aaccagcacc tgcggcgaga gggctacacc gtgcaggtga acgtgaacga ctatctggat 180
atttactgcc cgcactacaa cagctcgggg gtgggcccgg gggcgggagc ggggcccgga 240
ggcggggcag agcagtacgt gctgtacatg gtgagccgca acggctaccg cacctgcaac 300
gccagccagg gcttcaagcg ctgggagtgc aaccggccgc acgccccgca cagccccatc 360
aagttctcgg agaagttcca gcgctacagc gccttctctc tgggctacga gttccacgcc 420
ggccacgagt actactacat ctccacgccc actcacaacc tgcactggaa gtgtctgagg 480
atgaaggtgt tcgtctgctg cgcctccaca tcgcactccg gggagaagcc ggtccccact 540
ctccccagt tcaccatggg ccccaatatg aagatcaacg tgctggaaga ctttgaggga 600
gagaaccctc aggtgcccaa gcttgagaag agcatcagcg ggaccagccc caaacgggaa 660
cacctgcccc tggccgtggg catcgccttc ttcctcatga cgttcttggc ctcctag 717

<210> 19
<211> 606

<212> DNA
<213> Homo sapiens

<300>
<302> ephrin-A3
<310> XM001784

<400> 19
atgcggctgc tgcccctgct gcggactgtc ctctgggccg cgttcctcgg ctcccctctg 60
cgcgggggct ccagcctccg ccacgtagtc tactggaact ccagtaaccc caggttgctt 120
cgaggagacg ccgtggtgga gctgggcctc aacgattacc tagacattgt ctgcccccac 180
tacgaaggcc cagggccccc tgagggcccc gagacgtttg ctttgtacat ggtggactgg 240
ccaggctatg agtcctgcca ggcagagggc ccccgggcct acaagcgctg ggtgtgctcc 300
ctgccctttg gccatgttca attctcagag aagattcagc gcttcacacc cttctccctc 360
ggctttgagt tcttacctgg agagacttac tactacatct cggtgcccac tccagagagt 420
tctggccagt gcttgaggct ccaggtgtct gtctgctgca aggagaggaa gtctgagtca 480
gcccatcctg ttgggagccc tggagagagt ggcacatcag ggtggcgagg gggggacact 540
cccagccccc tctgtctctt gctattactg ctgctttctga ttcttcgtct tctgcgaatt 600
ctgtga 606

<210> 20
<211> 687
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin-A5
<310> NM001962

<400> 20
atgttgcacg tggagatgtt gacgctggtg tttctggtgc tctggatgtg tgtgttcagc 60
caggacccgg gctccaaggc cgtcgccgac cgctacgctg tctactggaa cagcagcaac 120
cccagattcc agaggggtga ctaccatatt gatgtctgta tcaatgacta cctggatgtt 180
ttctgccctc actatgagga ctccgtccca gaagataaga ctgagcgcta tgtcctctac 240
atggtgaact ttgatggcta cagtgcctgc gaccacactt ccaaagggtt caagagatgg 300
gaatgtaacc ggcctcactc tccaaatgga ccgctgaagt tctctgaaaa attccagctc 360
ttcactcctt tttctctagg atttgaattc aggccaggcc gagaatattt ctacatctcc 420
tctgcaatcc cagataatgg aagaaggtcc tgtctaaagc tcaaagtctt tgtgagacca 480
acaaatagct gtatgaaaac tataggtgtt catgatcgtg ttttcgatgt taacgacaaa 540
gtagaaaatt cattagaacc agcagatgac accgtacatg agtcagccga gccatcccgc 600
ggcgagaacg cggcacaaac accaaggata cccagccgcc ttttggcaat cctactgttc 660
ctcctggcga tgcttttgac attatag 687

<210> 21
<211> 2955
<212> DNA
<213> Homo sapiens

<400> 21
atggccctgg attatctact actgctcctc ctggcatccg cagtggctgc gatggaagaa 60
acgttaatgg acaccagaac ggctactgca gagctgggct ggacggccaa tcctgcgtcc 120
gggtgggaag aagtcagtgg ctacgatgaa aacctgaaca ccatccgcac ctaccaggtg 180
tgcaatgtct tcgagcccaa ccagaacaat tggctgctca ccaccttcat caaccggcgg 240
ggggcccatc gcatctacac agagatgcgc ttcactgtga gagactgcag cagcctccct 300
aatgtcccag gatcctgcaa ggagaccttc aacttgtatt actatgagac tgactctgtc 360
attgccacca agaagtcagc cttctggtct gaggcccctc acctcaaagt agacaccatt 420
gctgcagatg agagcttctc ccaggtggac tttgggggaa ggctgatgaa ggtaaacaca 480
gaagtcagga gctttgggcc tcttactcgg aatggttttt acctcgcttt tcaggattat 540

ggagcctgta tgtctcttct ttctgtccgt gtcttcttca aaaagtgtcc cagcattgtg 600
caaaatttg cagtgtttcc agagactatg acaggggcag agagcacatc tctggtgatt 660
gctcgggaca catgcatccc caacgcagag gaagtggacg tgcccatcaa actctactgc 720
aacgggaatg gggaatggat ggtgcctatt gggcgatgca cctgcaagcc tggctatgag 780
cctgagaaca gcgtggcatg caaggcttgc cctgcaggga cattcaaggc cagccaggaa 840
gctgaaggct gctcccactg cccctccaac agccgctccc ctgcagaggc gtctccatc 900
tgcacctgtc ggaccggtta ttaccgagcg gactttgacc ctccagaagt ggcatgcact 960
agcgtcccat caggtccccg caatgttatc tccatcgtca atgagacgtc catcatttctg 1020
gagtggcacc ctccaaggga gacaggtggg cgggatgatg tgacctacaa catcatctgc 1080
aaaaagtgcc gggcagaccg ccggagctgc tcccgctgtg acgacaatgt ggagtttgtg 1140
cccaggcagc tgggcctgac ggagtgccgc gtctccatca gcagcctgtg ggcccacacc 1200
ccctacacct ttgacatcca ggccatcaat ggagtctcca gcaagagtcc cttcccccca 1260
cagcacgtct ctgtcaacat caccacaaac caagccgccc cctccaccgt tcccatcatg 1320
caccaagtca gtgccactat gaggagcatc accttgtcat ggccacagcc ggagcagccc 1380
aatggcatca tcctggacta tgagatccgg tactatgaga aggaacacaa tgagttcaac 1440
tcctccatgg ccaggagtca gaccaacaca gcaaggattg atgggctgcg gcctggcatg 1500
gtatatgtgg tacaggtgcg tgcccgcact gttgctggct acggcaagtt cagtggcaag 1560
atgtgcttcc agactctgac tgacgatgat tacaagtcag agctgaggga gcagctgccc 1620
ctgattgctg gctcggcagc ggccggggtc gtgttcgttg tgtccttggt ggccatctct 1680
atcgtctgta gcaggaaacg ggcttatagc aaagaggctg tgtacagcga taagctccag 1740
cattacagca caggccgagg ctccccaggg atgaagatct acattgaccc cttcacttat 1800
gaggatccca acgaagctgt ccgggagttt gccaaggaga ttgatgtatc ttttgtgaaa 1860
attgaagagg tcatcggagc agcggagttt ggagaagtgt acaaggggcg tttgaaactg 1920
ccaggcaaga gggaaatcta cgtggccatc aagaccctga aggcagggta ctcggagaag 1980
cagcgtcggg actttctgag tgaggcgagc atcatgggcc agttcgacca tcctaacatc 2040
attcgcctgg agggtgtggt caccaagagt cggcctgtca tgatcatcac agagttcatg 2100
gagaatggtg cattggattc tttcctcagg caaaatgacg ggcagttcac cgtgatccag 2160
cttgtgggta tgctcagggg catcgctgct ggcatgaagt acctggctga gatgaattat 2220
gtgcatcggg acctggctgc taggaacatt ctggtcaaca gtaacctggt gtgcaaggtg 2280
tccgactttg gcctctccg ctacctccag gatgacacct cagatcccac ctacaccagc 2340
tccttgggag ggaagatccc tgtgagatgg acagctccag aggccatcgc ctaccgcaag 2400
ttcacttcag ccagcgacgt ttggagctat gggatcgtca tgtgggaagt catgtcattt 2460
ggagagagac cctattggga tatgtccaac caagatgtca tcaatgccat cgagcaggac 2520
taccggctgc ccccacccat ggactgtcca gctgctctac accagctcat gctggactgt 2580
tggcagaagg accggaacag ccggccccgg tttgcggaga ttgtcaacac cctagataag 2640
atgatccgga acccggcaag tctcaagact gtggcaacca tcaccgccgt gccttcccag 2700
cccctgctcg accgctccat cccagacttc acggcctttа ccaccgtgga tgactggctc 2760
agcgccatca aaatggtcca gtacagggac agcttcctca ctgctggctt cacctccctc 2820
cagctggtca cccagatgac atcagaagac ctcctgagaa taggcatcac cttggcaggc 2880
catcagaaga agatcctgaa cagcattcat tctatgaggg tccagataag tcagtcacca 2940
acggcaatgg catga 2955

<210> 22
<211> 3168
<212> DNA
<213> Homo sapiens

<400> 22
atggctctgc ggaggctggg ggccgcgctg ctgctgctgc cgctgctcgc cgccgtggaa 60
gaaacgctaa tggactccac tacagcgact gctgagctgg gctggatggt gcatcctcca 120
tcagggtggg aagaggtgag tggctacgat gagaacatga acacgatccg cacgtaccag 180
gtgtgcaacg tgtttgagtc aagccagaac aactggctac ggaccaagtt tatccggcgc 240
cgtggcgccc accgcatcca cgtggagatg aagttttcgg tgcgtgactg cagcagcatc 300
cccagcgtgc ctggctcctg caaggagacc ttcaacctct attactatga ggctgacttt 360
gactcggcca ccaagacctt ccccaactgg atggagaatc catgggtgaa ggtggatacc 420
attgcagccg acgagagctt ctcccaggtg gacctgggtg gccgcgtcat gaaaatcaac 480
accgaggtgc ggagcttcgg acctgtgtcc cgcagcggct tctacctggc cttccaggac 540
tatggcggct gcatgtccct catcgccgtg cgtgtcttct accgcaagtg ccccccgatc 600
atccagaatg gcgccatctt ccaggaaacc ctgtcgggag ctgagagcac atcgctggtg 660

gctgcccggg gcagctgcat cgccaatgcg gaagaggtgg atgtacccat caagctctac 720
tgtaacgggg acggcgagtg gctggtgccc atcgggcgct gcatgtgcaa agcaggcttc 780
gaggccgttg agaatggcac cgtctgccga ggttgtccat ctgggacttt caaggccaac 840
caaggggatg aggcctgtac ccactgtccc atcaacagcc ggaccacttc tgaaggggcc 900
accaactgtg tctgccgcaa tggctactac agagcagacc tggaccccct ggacatgccc 960
tgcacaacca tcccctccgc gccccaggct gtgatttcca gtgtcaatga gacctccctc 1020
atgctggagt ggaccccctcc ccgcgactcc ggaggccgag aggacctcgt ctacaacatc 1080
atctgcaaga gctgtggctc gggccggggt gcctgcaccc gctgcgggga caatgtacag 1140
tacgcaccac gccagctagg cctgaccgag ccacgcattt acatcagtga cctgctggcc 1200
cacacccagt acaccttcga gatccaggct gtgaacggcg ttactgacca gagccccttc 1260
tcgcctcagt tcgccttctgt gaacatcacc accaaccagg cagctccatc ggcagtgtcc 1320
atcatgcatc aggtgagccg caccgtggac agcattaccc tgtcgtggtc ccagccagac 1380
cagcccaatg gcgtgatcct ggactatgag ctgcagtact atgagaagga gctcagtgag 1440
tacaacgcca cagccataaa aagccccacc aacacggtca ccgtgcaggg cctcaacagc 1500
ggcgccatct atgtcttcca ggtgcgggca cgcaccgtgg caggctacgg gcgctacagc 1560
ggcaagatgt acttccagac catgacagaa gccgagtacc agacaagcat ccaggagaag 1620
ttgccactca tcatcggctc ctcggccgct ggctcggtct tcctcattgc tgtggttgtc 1680
atcgccatcg tgtgtaacag acgggggttt gagcgtgctg actcggagta cacggacaag 1740
ctgcaacact acaccagtgg ccacatgacc ccaggcatga agatctacat cgatcctttc 1800
acctacgagg accccaacga ggcagtgcgg gagtttgcca aggaaattga catctcctgt 1860
gtcaaaattg agcaggtgat cggagcaggg gagtttggcg aggtctgcag tggccacctg 1920
aagctgccag gcaagagaga gatctttgtg gccatcaaga cgctcaagtc gggctacacg 1980
gagaagcagc gccgggactt cctgagcgaa gcctccatca tgggccagtt cgaccatccc 2040
aacgtcatcc acctggaggg tgtcgtgacc aagagcacac ctgtgatgat catcaccgag 2100
ttcatggaga atggctccct ggactccttt ctccggcaaa acgatgggca gttcacagtc 2160
atccagctgg tgggcatgct tcggggcatc gcagctggca tgaagtacct ggcagacatg 2220
aactatgttc accgtgacct ggctgcccgc aacatcctcg tcaacagcaa cctggtctgc 2280
aaggtgtcgg actttgggct ctcacgcttt ctagaggacg atacctcaga ccccacctac 2340
accagtgccc tgggcggaaa gatccccatc cgctggacag ccccggaagc catccagtac 2400
cggaagttca cctcggccag tgatgtgtgg agctacggca ttgtcatgtg ggaggtgatg 2460
tcctatgggg agcggcccta ctgggacatg accaaccagg atgtaatcaa tgccattgag 2520
caggactatc ggctgccacc gcccatggac tgcccgagcg ccctgcacca actcatgctg 2580
gactgttggc agaaggaccg caaccaccgg cccaagttcg gccaaattgt caacacgcta 2640
gacaagatga tccgcaatcc caacagcctc aaagccatgg cgccctctc ctctggcatc 2700
aacctgccgc tgctggaccg cacgatcccc gactacacca gctttaacac ggtggacgag 2760
tggctggagg ccatcaagat ggggcagtac aaggagagct tcgccaatgc cggcttcacc 2820
tcctttgacg tcgtgtctca gatgatgatg gaggacattc tccgggttgg ggtcactttg 2880
gctggccacc agaaaaaaat cctgaacagt atccaggtga tgcgggcgca gatgaaccag 2940
attcagtctg tggagggcca gccactcgcc aggaggccac gggccacggg aagaaccaag 3000
cggtgccagc cacgagacgt caccaagaaa acatgcaact caaacgacgg aaaaaaaaag 3060
ggaatgggaa aaaagaaaac agatcctggg agggggcggg aaatacaagg aatatttttt 3120
aaagaggatt ctcataagga aagcaatgac tgttcttgcg ggggataa 3168

<210> 23
<211> 2997
<212> DNA
<213> Homo sapiens

<400> 23
atggccagag cccgcccgcc gccgccgccg tcgccgccgc cggggcttct gccgctgctc 60
cctccgctgc tgctgctgcc gctgctgctg ctgcccgccg gctgccgggc gctggaagag 120
accctcatgg acacaaaatg ggtaacatct gagttggcgt ggacatctca tccagaaagt 180
gggtgggaag aggtgagtgg ctacgatgag gccatgaatc ccatccgcac ataccaggtg 240
tgtaatgtgc gcgagtcaag ccagaacaac tggcttcgca ccggggttcat ctggcggcgg 300
gatgtgcagc gggtctacgt ggagctcaag ttcactgtgc gtgactgcaa cagcatcccc 360
aacatccccg gctcctgcaa ggagaccttc aacctcttct actacgaggc tgacagcgat 420
gtggcctcag cctcctccct cttctggatg gagaacccct acgtgaaagt cgaaaccatt 480
gcacccgatg agagcttctc gcggctggat gccggccgtg tcaacaccaa ggtgcgcagc 540
tttgggccac tttccaaggc tggcttctac ctggccttcc aggaccaggg cgcctgcatg 600

tcgctcatct ccgtgcgcgc cttctacaag aagtgtgcat ccaccaccgc aggcttcgca 660
ctctttcccg agaccctcac tggggcggag cccacctcgc tggtcattgc tcctggcacc 720
tgcatccctа acgccgtgga ggtgtcggtg ccactcaagc tctactgcaa cggcgatggg 780
gagtggatgg tgcctgtggg tgcctgcacc tgtgccaccg gcatggagcc agctgccaag 840
gagtcccagt gccgcccctg tcccctggg agctacaagg cgaagcaggg agaggggccc 900
tgcctcccat gtcccccaa cagccgtacc acctccccag ccgccagcat ctgccactgc 960
cacaataact tctaccgtgc agactcggac tctgcggaca gtgcctgtac caccgtgcca 1020
tctccacccc gaggtgtgat ctccaatgtg aatgaaacct cactgatcct cgagtggagt 1080
gagccccggg acctgggtgt ccgggatgac ctcctgtaca atgtcatctg caagaagtgc 1140
catgggggctg gaggggcctc agcctgctca cgctgtgatg acaacgtgga gtttgtgcct 1200
cggcagctgg gcctgtcgga gccccgggtc cacaccagcc atctgctggc ccacacgcgc 1260
tacacctttg aggtgcaggc ggtcaacggt gtctcgggca agagccctct gccgcctcgt 1320
tatgcggccg tgaatatcac cacaaaccag gctgccccgt ctgaagtgcc cacactacgc 1380
ctgcacagca gctcaggcag cagcctcacc ctatcctggg caccccaga gcggccaac 1440
ggagtcatcc tggactacga gatgaagtac tttgagaaga gcgagggcat cgcctccaca 1500
gtgaccagcc agatgaactc cgtgcagctg gacgggcttc ggcctgacgc cgctatgtg 1560
gtccaggtcc gtgcccgcac agtagctggc tatgggcagt acagccgccc tgccgagttt 1620
gagaccacaa gtgagagagg ctctgggccc cagcagctcc aggagcagct tcccctcatc 1680
gtgggctccg ctacagctgg gcttgtcttc gtggtggctg tcgtggtcat cgctatcgtc 1740
tgcctcagga agcagcgaca cggctctgat tcggagtaca cggagaagct gcagcagtac 1800
attgctcctg gaatgaaggt ttatattgac ccttttacct acgaggaccc taatgaggct 1860
gttcgggagt ttgccaagga gatcgacgtg tcctgcgtca agatcgagga ggtgatcgga 1920
gctgggaat ttggggaagt gtgccgtggt cgactgaaac agcctggccg ccgagaggtg 1980
tttgtggcca tcaagacgct gaaggtgggc tacaccgaga ggcagcggcg ggacttccta 2040
agcgaggcct ccatcatggg tcagtttgat cacccaata taatccggct cgaggggctg 2100
gtcaccaaaa gtcggccagt tatgatcctc actgagttca tggaaaactg cgccctggac 2160
tccttcctcc ggctcaacga tgggcagttc acggtcatcc agctggtggg catgttgcgg 2220
ggcattgctg ccggcatgaa gtacctgtcc gagatgaact atgtgcaccg cgacctggct 2280
gctcgcaaca tccttgtcaa cagcaacctg gtctgcaaag tctcagactt tggcctctcc 2340
cgcttcctgg aggatgaccc ctccgatcct acctacacca gttccctggg cgggaagatc 2400
cccatccgct ggactgcccc agaggccata gcctatcgga agttcacttc tgctagtgat 2460
gtctggagct acggaattgt catgtgggag gtcatgagct atggagagcg accctactgg 2520
gacatgagca accaggatgt catcaatgcc gtggagcagg attaccggct gccaccaccc 2580
atggactgtc ccacagcact gcaccagctc atgctggact gctgggtgcg ggaccggaac 2640
ctcaggccca aattctccca gattgtcaat accctggaca agctcatccg caatgctgcc 2700
agcctcaagg tcattgccag cgctcagtct ggcatgtcac agccctcctc ggaccgcacg 2760
gtcccagatt acacaacctt cacgacagtt ggtgattggc tggatgccat caagatgggg 2820
cggtacaagg agagcttcgt cagtgcgggg tttgcatctt ttgacctggt ggccccagatg 2880
acggcagaag acctgctccg tattggggtc accctggccg gccaccagaa gaagatcctg 2940
agcagtatcc aggacatgcg gctgcagatg aaccagacgc tgcctgtgca ggtctga 2997

<210> 24
<211> 2964
<212> DNA
<213> Homo sapiens

<400> 24
atggagctcc gggtgctgct ctgctgggct tcgttggccg cagctttgga agagaccctg 60
ctgaacacaa aattggaaac tgctgatctg aagtgggtga cattccctca ggtggacggg 120
cagtggagg aactgagcgg cctggatgag gaacagcaca gcgtgcgcac ctacgaagtg 180
tgtgaagtgc agcgtgccc gggccaggcc cactggcttc gcacaggttg ggtcccacgg 240
cggggcgccg tccacgtgta cgccacgctg cgcttcacca tgctcgagtg cctgtccctg 300
cctcgggctg ggcgctcctg caaggagacc ttcaccgtct tctactatga gagcgatgcg 360
gacacggcca cggccctcac gccagcctgg atggagaacc cctacatcaa ggtggacacg 420
gtggccgcgg agcatctcac ccggaagcgc cctgggtccg aggccaccgg gaaggtgaat 480
gtcaagacgc tgcgtctggg accgctcagc aaggctggct tctacctggc cttccaggac 540
cagggtgcct gcatggccct gctatcctg cacctcttct acaaaaagtg cgcccagctg 600
actgtgaacc tgactcgatt cccggagact gtgcctcggg agctggttgt gcccgtggcc 660
ggtagctgcg tggtggatgc cgtccccgcc cctggccca gccccagcct ctactgccgt 720

gaggatggcc agtgggccga acagccggtc acgggctgca gctgtgctcc ggggttcgag 780
gcagctgagg ggaacaccaa gtgccgagcc tgtgcccagg gcaccttcaa gccctgtca 840
ggagaagggt cctgccagcc atgcccagcc aatagccact ctaacaccat tggatctgcc 900
gtctgccagt gccgcgtcgg ggacttccgg gcacgcacag acccccgggg tgcaccctgc 960
accacccctc cttcggctcc gcggagcgtg gtttcccgcc tgaacggctc ctccctgcac 1020
ctggaatgga gtgcccccct ggagtctggt ggccgagagg acctcaccta cgccctccgc 1080
tgccgggagt gccgacccgg aggctcctgt gcgccctgcg ggggagacct gacttttgac 1140
cccggccccc gggacctggt ggagccctgg gtggtggttc gagggctacg tccggacttc 1200
acctatacct ttgaggtcac tgcattgaac ggggtatcct ccttagccac ggggcccgtc 1260
ccatttgagc ctgtcaatgt caccactgac cgagaggtac ctcctgcagt gtctgacatc 1320
cgggtgacgc ggtcctcacc cagcagcttg agcctggcct gggctgttcc ccgggcaccc 1380
agtggggcgt ggctggacta cgaggtcaaa taccatgaga agggcgccga gggtcccagc 1440
agcgtgcggt tcctgaagac gtcagaaaac cgggcagagc tgcgggggct gaagcgggga 1500
gccagctacc tggtgcaggt acgggcgcgc tctgaggccg gctacgggcc cttcggccag 1560
gaacatcaca gccagaccca actggatgag agcgagggct ggcgggagca gctggccctg 1620
attgcgggca cggcagtcgt gggtgtggtc ctggtcattgt tggtcagttt 1680
ctctgcctca ggaagcagag caatgggaga gaagcagaat attcggacaa acacggacag 1740
tatctcatcg gacatggtac taaggtctac atcgacccct tcacttatga agacctaat 1800
gaggctgtga gggaatttgc aaaagagatc gatgtctcct acgtcaagat tgaagaggtg 1860
attggtgcag gtgagtttgg cgaggtgtgc cgggggcggc tcaaggcccc agggaagaag 1920
gagagctgtg tggcaatcaa gaccctgaag ggtggctaca cggagcggca gcggcgtgag 1980
tttctgagcg aggcctccat catgggccag ttcgagcacc ccaatatcat ccgcctggag 2040
ggcgtggtca ccaacagcat gcccgtcatg attctcacag agttcatgga gaacggcgcc 2100
ctggactcct tcctgcggct aaacgacgga cagttcacag tcatccagct cgtgggcatg 2160
ctgcggggca tcgcctcggg catgcggtac cttgccgaga tgagctacgt ccaccgagac 2220
ctggctgctc gcaacatcct agtcaacagc aacctcgtct gcaaagtgtc tgactttggc 2280
ctttcccgat tcctggagga gaactcttcc gatcccacct acacgagctc cctgggagga 2340
aagattccca tccgatggac tgccccggag gccattgcct tccggaagtt cactccgcc 2400
agtgatgcct ggagttacgg gattgtgatg tgggaggtga tgtcatttgg ggagaggccg 2460
tactggqaca tgagcaatca ggacgtgatc aatgccattg aacaggacta ccggctgccc 2520
ccgccccag actgtcccac ctccctccac cagctcatgc tggactgttg gcagaaagac 2580
cggaatgccc ggccccgctt ccccaggtg gtcagcgccc tggacaagat gatccggaac 2640
cccgccagcc tcaaaatcgt ggcccggag aatggcgggg cctcacaccc tctcctggac 2700
cagcggcagc ctcactactc agcttttggc tctgtgggcg agtggcttcg ggccatcaaa 2760
atggaagat acgaagccg tttcgcagcc gctggctttg gctccttcga gctggtcagc 2820
cagatctctg ctgaggacct gctccgaatc ggagtcactc tggcgggaca ccagaagaaa 2880
atcttggcca gtgtccagca catgaagtcc caggccaagc cgggaacccc gggtgggaca 2940
ggaggaccgg ccccgcagta ctga 2964

<210> 25
<211> 1041
<212> DNA
<213> Homo sapiens

<300>
<302> ephrin-B1
<310> NM004429

<400> 25
atggctcggc ctgggcagcg ttggctcggc aagtggcttg tggcgatggt cgtgtgggcg 60
ctgtgccggc tcgccacacc gctggccaag aacctggagc ccgtatcctg gagctccctc 120
aaccccaagt tcctgagtgg gaagggcttg gtgatctatc cgaaaattgg agacaagctg 180
gacatcatct gccccgagc agaagcaggg cggccctatg agtactacaa gctgtacctg 240
gtgcggcctg agcaggcagc tgcctgtagc acagttctcg accccaacgt gttggtcacc 300
tgcaataggc cagagcagga aatacgcttt accatcaagt tccaggagtt cagccccaac 360
tacatgggcc tggagttcaa gaagcaccat gattactaca ttacctcaac atccaatgga 420
agcctggagg ggctggaaaa ccgggagggc ggtgtgtgcc gcacacgcac catgaagatc 480
atcatgaagg ttgggcaaga tcccaatgct gtgacgcctg agcagctgac taccagcagg 540
cccagcaagg aggcagacaa cactgtcaag atggccacac aggcccctgg tagtcggggc 600

tccctgggtg actctgatgg caagcatgag actgtgaacc aggaagagaa gagtggccca 660
ggtgcaagtg ggggcagcag cggggaccct gatggcttct tcaactccaa ggtggcattg 720
ttcgcggctg tcggtgccgg ttgcgtcatc ttcctgctca tcatcatctt cctgacggtc 780
ctactactga agctacgcaa gcggcaccgc aagcacacac agcagcgggc ggctgccctc 840
tcgctcagta ccctggccag tcccaagggg ggcagtggca cagcgggcac cgagcccagc 900
gacatcatca ttcccttacg gactacagag aacaactact gcccccacta tgagaaggtg 960
agtggggact acgggcaccc tgtctacatc gtccaagaga tgccgcccca gagcccggcg 1020
aacatctact acaaggtctg a 1041

<210> 26
<211> 1002
<212> DNA
<213> Homo sapiens

<300>

<400> 26
atggctgtga gaagggactc cgtgtggaag tactgctggg gtgttttgat ggttttatgc 60
agaactgcga tttccaaatc gatagtttta gagcctatct attggaattc ctcgaactcc 120
aaatttctac ctggacaagg actggtacta tacccacaga taggagacaa attggatatt 180
atttgcccca aagtggactc taaaactgtt ggccagtatg aatattataa agttttatg 240
gttgataaag accaagcaga cagatgcact attaagaagg aaaatacccc tctcctcaac 300
tgtgccaaac cagaccaaga tatcaaattc accatcaagt ttcaagaatt cagccctaac 360
ctctgggggtc tagaatttca gaagaacaaa gattattaca ttatatctac atcaaatggg 420
tctttggagg gcctggataa ccaggaggga ggggtgtgcc agacaagagc catgaagatc 480
ctcatgaaag ttggacaagt tgcaagttct gctggatcaa ccaggaataa agatccaaca 540
agacgtccag aactagaagc tggtacaaat ggaagaagtt cgacaacaag tcctttgta 600
aaaccaaatc caggttctag cacagacggc aacagcgccg gacattcggg gaacaacatc 660
ctcggttccg aagtggcctt atttgcaggg attgcttcag gatgcatcat cttcatcgtc 720
atcatcatca cgctggtggt cctcttgctg aagtaccgga ggagacacag gaagcactcg 780
ccgcagcaca cgaccacgct gtcgctcagc acactggcca cacccaagcg cagcggcaac 840
aacaacggct cagagcccag tgacattatc atcccgctaa ggactgcgga cagcgtcttc 900
tgccctcact acgagaaggt cagcggcgac tacgggcacc cggtgtacat cgtccaggag 960
atgccccgc agagcccggc gaacatttac tacaaggtct ga 1002

<210> 27
<211> 1023
<212> DNA
<213> Homo sapiens

<400> 27
atggggcccc cccattctgg gccggggggc gtgcgagtcg gggccctgct gctgctgggg 60
gttttggggc tggtgtctgg gctcagcctg gagcctgtct actggaactc ggcgaataag 120
aggttccagg cagagggtgg ttatgtgctg taccctcaga tcggggaccg gctagacctg 180
ctctgccccc gggccggcc tcctggccct cactcctctc ctaattatga gttctacaag 240
ctgtacctgg taggggtgtgc tcagggccgg cgctgtgagg caccccctgc cccaaacctc 300
cttctcactt gtgatcgccc agacctggat ctccgcttca ccatcaagtt ccaggagtat 360
agccctaatc tctggggcca cgagttccgc tcgcaccacg attactacat cattgccaca 420
tcggatggga cccgggaggg cctggagagc ctgcagggag gtgtgtgcct aaccagaggc 480
atgaaggtgc ttctccgagt gggacaaagt ccccgaggag gggctgtccc ccgaaaacct 540
gtgtctgaaa tgcccatgga aagagaccga ggggcagccc acagcctgga gcctgggaag 600
gagaacctgc caggtgaccc caccagcaat gcaacctccc ggggtgctga agggcccctg 660
ccccctccca gcatggctgc agtggctggg gcagcagggg ggctgggcgt gctcttgctg 720
ggcgtggcag gggctggggg tgccatgtgt tggcgggagac ggcgggccaa gccttcggag 780
agtcgccacc ctggtcctgg ctccttcggg aggggagggt ctctgggcct gggggtgga 840
ggtgggatgg gacctcggga ggctgagcct ggggagctag ggatagctct gcgggggtggc 900
ggggctgcag atcccccctt ctgcccccac tatgagaagg tgagtggtga ctatgggcat 960
cctgtgtata tcgtgcagga tgggcccccc cagagccctc caaacatcta ctacaaggta 1020

tga 1023

<210> 28
<211> 3399
<212> DNA
<213> Homo sapiens

<300>
<302> telomerase reverse transcriptase
<310> AF015950

<400> 28
atgccgcgcg ctccccgctg ccgagccgtg cgctccctgc tgcgcagcca ctaccgcgag 60
gtgctgccgc tggccacgtt cgtgcggcgc ctggggcccc agggctggcg gctggtgcag 120
cgcggggacc cggcggcttt ccgcgcgctg gtggcccagt gcctggtgtg cgtgccctgg 180
gacgcacggc cgccccccgc cgcccctctc ttccgccagg tgtcctgcct gaaggagctg 240
gtggcccgag tgctgcagag gctgtgcgag cgcggccgca agaacgtgct ggccttcggc 300
ttcgcgctgc tggacggggc ccgcgggggc ccccccgagg ccttcaccac cagcgtgcgc 360
agctacctgc ccaacacggt gaccgacgca ctgcgggggа gcgggggctg ggggctgctg 420
ctgcgccgcg tgggcgacga cgtgctggtt cacctgctgg cacgctgcgc gctcttttgtg 480
ctggtggctc ccagctgcgc ctaccaggtg tgcgggccgc cgctgtacca gctcggcgct 540
gccactcagg cccggccccc gccacacgct agtggacccc gaaggcgtct gggatgcgaa 600
cgggcctgga accatagcgt cagggaggcc ggggtccccc tgggcctgcc agccccgggt 660
gcgaggaggc gcgggggcag tgccagccga agtctgccgt tgcccaagag gcccaggcgt 720
ggcgctgccc ctgagccgga gcggacgccc gttgggcagg ggtcctgggc ccacccgggc 780
aggacggctg gaccgagtga ccgtggtttc tgtgtggtgt cacctgccag acccgccgaa 840
gaagccacct ctttggaggg tgcgctctct ggcacgcgcc actcccaccc atccgtgggc 900
cgccagcacc acgcgggccc cccatccaca tcgcggccac cacgtccctg ggacacgcct 960
tgtcccccgg tgtacgccga gaccaagcac ttcctctact cctcaggcga caaggagcag 1020
ctgcggccct ccttcctact cagctctctg aggcccagcc tgactggcgc tcggaggctc 1080
gtggagacca tctttctggg ttccaggccc tggatgccag ggactcccag caggttgccc 1140
cgcctgcccc agcgctactg gcaaatgcgg ccctcgtttc tggagctgct tgggaaccac 1200
gcgcagtgcc cctacggggt gctcctcaag acgcactgcc cgctgcgagc tgcggtcacc 1260
ccagcagccg gtgtctgtgc ccgggagaag ccccagggct ctgtggcggc ccccgaggag 1320
gaggacacag accccgtccg cctggtgcag ctgctccgcc agcacagcag ccccctggcag 1380
gtgtacggct tcgtgcgggc ctgcctgcgc cggctggtgc ccccaggcct ctgggctcc 1440
aggcacaacg aacgccgctt cctcaggaac accaagaagt tcatctccct ggggaagcat 1500
gccaagctct cgctgcagga gctgacgtgg aagatgagcg tgcgggactg cgcttggctg 1560
cgcaggagcc cagggggttgg ctgtgttccg gccgcagagc accgtctgcg tgaggagatc 1620
ctggccaagt tcctgcactg gctgatgagt gtgtacgtcg tcgagctgct caggtctttc 1680
ttttatgtca cggagaccac gtttcaaaag aacaggctct ttttctaccg gaagagtgtc 1740
tggagcaagt tgcaaagcat tggaatcaga cagcacttga agagggtgca gctgcgggag 1800
ctgtcggaag cagaggtcag gcagcatcgg gaagccaggc ccgccctgct gacgtccaga 1860
ctccgcttca tccccaagcc tgacgggctg cggccgattg tgaacatgga ctacgtcgtg 1920
ggagccagaa cgttccgcag agaaaagagg gccgagcgtc tcacctcgag ggtgaaggca 1980
ctgttcagcg tgctcaacta cgagcgggcg cggcgcccg gcctcctggg cgcctctgtg 2040
ctgggcctgg acgatatcca cagggcctgg cgcaccttcg tgctgcgtgt gcgggcccag 2100
gacccgccgc ctgagctgta ctttgtcaag gtggatgtga cgggcgcgta cgacaccatc 2160
ccccaggaca ggctcacgga ggtcatcgcc agcatcatca aacccacgaa cacgtactgc 2220
gtgcgtcggt atgccgtggt ccagaaggcc gcccatgggc acgtccgcaa ggcctttcaag 2280
agccacgtct ctaccttgac agacctccag ccgtacatgc gacagttcgt ggctcacctg 2340
caggagacca gcccgctgag ggatgccgtc gtcatcgagc agagctcctc cctgaatgag 2400
gccagcagtg gcctctttga cgtcttcctа cgcttcatgt gccacacgcc cgtgcgcatc 2460
agggcaagt cctacgtcca gtgccagggg atcccgcagg gctccatcct ctccacgctg 2520
ctctgcagcc tgtgctacgg cgacatggag aacaagctgt ttgcggggat tcggcgggac 2580
gggctgctcc tgcgtttggt ggatgatttc ttgttggtga cacctcacct cacccacgcg 2640
aaaaccttcc tcaggaccct ggtccgaggt gtcccttgagt atggctgcgt ggtgaacttg 2700
cggaagacag tggtgaacтt ccctgtagaa gacgaggccc tgggtggcac ggcttttgtt 2760
cagatgccgg cccacggcct attccccttgg tgcggcctgc tgctggatac ccggaccctg 2820

gaggtgcaga gcgactactc cagctatgcc cggacctcca tcagagccag tctcaccttc 2880
aaccgcggct tcaaggctgg gaggaacatg cgtcgcaaac tctttggggt cttgcggctg 2940
aagtgtcaca gcctgtttct ggatttgcag gtgaacagcc tccagacggt gtgcaccaac 3000
atctacaaga tcctcctgct gcaggcgtac aggttttcacg catgtgtgct gcagctccca 3060
tttcatcagc aagtttggaa gaaccccaca ttttttctgc gcgtcatctc tgacacggcc 3120
tccctctgct actccatcct gaaagccaag aacgcaggga tgtcgctggg ggccaagggc 3180
gccgccggcc ctctgccctc cgaggccgtg cagtggctgt gccaccaagc attcctgctc 3240
aagctgactc gacaccgtgt cacctacgtg ccactcctgg ggtcactcag gacagcccag 3300
acgcagctga gtcggaagct cccggggacg acgctgactg ccctggaggc cgcagccaac 3360
ccggcactgc cctcagactt caagaccatc ctggactga 3399

<210> 29
<211> 567
<212> DNA
<213> Homo sapiens

<300>
<302> K-ras
<310> M54968

<400> 29
atgactgaat ataaacttgt ggtagttgga gcttgtggcg taggcaagag tgccttgacg 60
atacagctaa ttcagaatca ttttgtggac gaatatgatc caacaataga ggattcctac 120
aggaagcaag tagtaattga tggagaaacc tgtctcttgg atattctcga cacagcaggt 180
caagaggagt acagtgcaat gagggaccag tacatgagga ctggggaggg ctttctttgt 240
gtatttgcca taaataatac taaatcattt gaagatattc accattatag agaacaaatt 300
aaaagagtta aggactctga agatgtacct atggtcctag taggaaataa atgtgatttg 360
ccttctagaa cagtagacac aaaacaggct caggacttag caagaagtta tggaattcct 420
tttattgaaa catcagcaaa gacaagacag ggtgttgatg atgccttcta tacattagtt 480
cgagaaattc gaaaacataa agaaaagatg agcaaagatg gtaaaaagaa gaaaaagaag 540
tcaaagacaa agtgtgtaat tatgtaa 567

<210> 30
<211> 3840
<212> DNA
<213> Homo sapiens

<300>
<302> mdr-1
<310> AF016535

<400> 30
atggatcttg aaggggaccg caatggagga gcaaagaaga agaacttttt taaactgaac 60
aataaaagtg aaaaagataa gaaggaaaag aaaccaactg tcagtgtatt ttcaatgttt 120
cgctattcaa attggcttga caagttgtat atggtggtgg gaactttggc tgccatcatc 180
catggggctg gacttcctct catgatgctg gtgttttgag aaatgacaga tatctttgca 240
aatgcaggaa atttagaaga tctgatgtca aacatcacta atagaagtga tatcaatgat 300
acagggttct tcatgaatct ggaggaagac atgaccaggt atgcctatta ttacagtgga 360
attggtgctg gggtgctggt tgctgcttac attcaggttt cattttggtg cctggcagct 420
ggaagacaaa tacacaaaat tagaaaacag ttttttcatg ctataatgcg acaggagata 480
ggctggtttg atgtgcacga tgttggggag cttaacaccc gacttacaga tgatgtctcc 540
aagattaatg aaggaattgg tgacaaaatt ggaatgtttct ttcagtcaat ggcaacattt 600
ttcactgggt ttatagtagg atttacacgt ggttggaagc taacccttgt gattttggcc 660
atcagtcctg ttcttggact gtcagctgct gtctgggcaa agatactatc ttcatttact 720
gataaagaac tcttagcgta tgcaaaagct ggagcagtag ctgaagaggt cttggcagca 780
attagaactg tgattgcatt tggaggacaa aagaaagaac ttgaaaggta caacaaaaat 840
ttagaagaag ctaaaagaat tgggatаaag aaagctatta cagccaatat ttctatаggt 900
gctgctttcc tgctgatcta tgcatcttat gctctggcct tctggtatgg gaccaccttg 960

gtcctctcag gggaatattc tattggacaa gtactcactg tattttctgt attaattggg 1020
gcttttagtg ttggacaggc atctccaagc attgaagcat ttgcaaatgc aagaggagca 1080
gcttatgaaa tcttcaagat aattgataat aagccaagta ttgacagcta ttcgaagagt 1140
gggcacaaac cagataatat taagggaaat ttggaattca gaaatgttca cttcagttac 1200
ccatctcgaa aagaagttaa gatcttgaag ggtctgaacc tgaaggtgca gagtgggcag 1260
acggtggccc tggttggaaa cagtggctgt gggaagagca caacagtcca gctgatgcag 1320
aggctctatg accccacaga ggggatggtc agtgttgatg gacaggatat taggaccata 1380
aatgtaaggt ttctacggga aatcattggt gtggtgagtc aggaacctgt attgtttgcc 1440
accacgatag ctgaaaacat tcgctatggc cgtgaaaatg tcaccatgga tgagattgag 1500
aaagctgtca aggaagccaa tgcctatgac tttatcatga aactgcctca taaatttgac 1560
accctggttg gagagagagg ggcccagttg agtggtgggc agaagcagag gatcgccatt 1620
gcacgtgccc tggttcgcaa ccccaagatc ctcctgctgg atgaggccac gtcagccttg 1680
gacacagaaa gcgaagcagt ggttcaggtg gctctggata aggccagaaa aggtcggacc 1740
accattgtga tagctcatcg tttgtctaca gttcgtaatg ctgacgtcat cgctggtttc 1800
gatgatggag tcattgtgga gaaaggaaat catgatgaac tcatgaaaga gaaaggcatt 1860
tacttcaaac ttgtcacaat gcagacagca ggaaatgaag ttgaattaga aaatgcagct 1920
gatgaatcca aaagtgaaat tgatgccttg gaaatgtctt caaatgattc aagatccagt 1980
ctaataagaa aaagatcaac tcgtaggagt gtccgtggat cacaagccca agacagaaag 2040
cttagtacca aagaggctct ggatgaaagt atacctccag tttccttttg gaggattatg 2100
aagctaaatt taactgaatg gccttatttt gttgttggtg tattttgtgc cattataaat 2160
ggaggcctgc aaccagcatt tgcaataata ttttcaaaga ttataggggt ttttacaaga 2220
attgatgatc ctgaaacaaa acgacagaat agtaacttgt tttcactatt gtttctagcc 2280
cttggaatta tttcttttat tacatttttc cttcagggtt tcacatttgg caaagctgga 2340
gagatcctca ccaagcggct ccgatacatg gttttccgat ccatgctcag acaggatgtg 2400
agttggtttg atgaccctaa aaacaccact ggagcattga ctaccaggct cgccaatgat 2460
gctgctcaag ttaaaggggc tataggttcc aggcttgctg taattaccca gaatatagca 2520
aatcttggga caggaataat tatatccttc atctatggtt ggcaactaac actgttactc 2580
ttagcaattg tacccatcat tgcaatagca ggagttgttg aaatgaaaat gttgtctgga 2640
caagcactga aagataagaa agaactagaa ggtgctggga agatcgctac tgaagcaata 2700
gaaaacttcc gaaccgttgt ttctttgact caggagcaga agtttgaaca tatgtatgct 2760
cagagtttgc aggtaccata cagaaactct ttgaggaaag cacacatctt tggaattaca 2820
ttttccttca cccaggcaat gatgtatttt tcctatgctg gatgtttccg gtttggagcc 2880
tacttggtgg cacataaact catgagcttt gaggatgttc tgttagtatt ttcagctgtt 2940
gtctttggtg ccatggccgt ggggcaagtc agttcatttg ctcctgacta tgccaaagcc 3000
aaaatatcag cagcccacat catcatgatc attgaaaaaa ccccttttgat tgacagctac 3060
agcacggaag gcctaatgcc gaacacattg gaaggaaatg tcaacatttgg tgaagttgta 3120
ttcaactatc ccaccccgacc ggacatccca gtgcttcagg gactgagcct ggaggtgaag 3180
aaggggcaga cgctggctct ggtgggcagc agtggctgtg ggaagagcac agtggtcaag 3240
ctcctggagc ggttctacga ccccttggca gggaaagtgc tgcttgatgg caaagaaata 3300
aagcgactga atgttcagtg gctccgagca cacctgggca tcgtgtccca ggagcccatc 3360
ctgtttgact gcagcattgc tgagaacatt gcctatggag acaacagccg ggtggtgtca 3420
caggaagaga ttgtgagggc agcaaaggag gccaacatac atgccttcat cgagtcactg 3480
cctaataaat atagcactaa agtaggagac aaaggaactc agctctctgg tggccagaaa 3540
caacgcattg ccatagctcg tgcccttgtt agacagcctc atattttgct ttgtgatgaa 3600
gccacgtcag ctctggatac agaaagtgaa aaggttgtcc aagaagccct ggacaaagcc 3660
agagaaggcc gcacctgcat tgtgattgct caccgcctgt ccaccatcca gaatgcagac 3720
ttaatagtgg tgtttcagaa tggcagagtc aaggagcatg gcacgcatca gcagctgctg 3780
gcacagaaag gcatctattt ttcaatggtc agtgtccagg ctggaacaaa gcgccagtga 3840

<210> 31
<211> 1316
<212> DNA
<213> Homo sapiens

<300>
<302> UPAR (urokinase-type plasminogen activator receptor)
<310> XM009232

<400> 31

atgggtcacc cgccgctgct gccgctgctg ctgctgctcc acacctgcgt cccagcctct 60
tggggcctgc ggtgcatgca gtgtaagacc aacggggatt gccgtgtgga agagtgcgcc 120
ctgggacagg acctctgcag gaccacgatc gtgcgcttgt gggaagaagg agaagagctg 180
gagctggtgg agaaaagctg tacccactca gagaagacca acaggaccct gagctatcgg 240
actggcttga agatcaccag ccttaccgag gttgtgtgtg ggttagactt gtgcaaccag 300
ggcaactctg gccgggctgt cacctattcc cgaagccgtt acctcgaatg catttcctgt 360
ggctcatcag acatgagctg tgagaggggc cggcaccaga gcctgcagtg ccgcagccct 420
gaagaacagt gcctggatgt ggtgacccac tggatccagg aaggtgaaga agggcgtcca 480
aaggatgacc gccacctccg tggctgtggc taccttccgg gctgcccggg ctccaatggt 540
ttccacaaca acgacacctt ccacttcctg aaatgctgca acacccacaa atgcaacgag 600
ggcccaatcc tggagcttga aaatctgccg cagaatggcc gccagtgtta cagctgcaag 660
gggaacagca cccatggatg ctcctctgaa gagactttcc tcattgactg ccgaggcccc 720
atgaatcaat gtctggtagc caccggcact cacgaaccga aaaaccaaag ctatatggta 780
agaggctgtg caaccgcctc aatgtgccaa catgcccacc tgggtgacgc cttcagcatg 840
aaccacattg atgtctcctg ctgtactaaa agtggctgta accacccaga cctggatgtc 900
cagtaccgca gtgggctgc tcctcagcct ggccctgccc atctcagcct caccatcacc 960
ctgctaatga ctgccagact gtggggaggc actctcctct ggacctaaac ctgaaatccc 1020
cctctctgcc ctggctggat ccgggggacc cctttgccct tccctcggct ccccagccta 1080
cagacttgct gtgtgacctc aggccagtgt gccgacctct ctgggcctca gttttcccag 1140
ctatgaaaac agctatctca caaagttgtg tgaagcagaa gagaaaagct ggaggaaggc 1200
cgtgggccaa tgggagagct cttgttatta ttaatattgt tgccgctgtt gtgttgttgt 1260
tattaattaa tattcatatt atttatttta tacttacata aagattttgt accagtgg 1318

<210> 32
<211> 636
<212> DNA
<213> Homo sapiens

<300>
<302> Bak
<310> U16811

<400> 32
atggcttcgg ggcaaggccc aggtcctccc aggcaggagt gcggagagcc tgccctgccc 60
tctgcttctg aggagcaggt agcccaggac acagaggagg ttttccgcag ctacgttttt 120
taccgccatc agcaggaaca ggaggctgaa ggggtggctg cccctgccga cccagagatg 180
gtcaccttac ctctgcaacc tagcagcacc atggggcagg tgggacggca gctcgccatc 240
atcgggggacg acatcaaccg acgctatgac tcagagttcc agaccatgtt gcagcacctg 300
cagcccacgg cagagaatgc ctatgagtac ttcaccaaga ttgccaccag cctgtttgag 360
agtggcatca attggggccg tgtggtggct cttctgggct tcggctaccg tctggcccta 420
cacgtctacc agcatggcct gactggcttc ctaggccagg tgaccccgtt cgtggtcgac 480
ttcatgctgc atcactgcat tgccccggtgg attgcacaga ggggtggctg ggtggcagcc 540
gtgaacttgg gcaatggtcc catcctgaac gtgctggtgg ttctgggtgt ggttctgttg 600
ggccagtttg tggtacgaag attcttcaaa tcatga 636

<210> 33
<211> 579
<212> DNA
<213> Homo sapiens

<300>
<302> Bax alpha
<310> L22473

<400> 33
atggacgggt ccggggagca gcccagaggc gggggcccca ccagctctga gcagatcatg 60
aagacagggg ccctttgct tcagggtttc atccaggatc gagcagggcg aatgggggg 120
gaggcaccg agctggccct ggacccggtg cctcaggatg cgtccaccaa gaagctgagc 180

gagtgtctca agcgcatcgg ggacgaactg gacagtaaca tggagctgca gaggatgatt 240
gccgccgtgg acacagactc cccccgagag gtcttttttcc gagtggcagc tgacatgttt 300
tctgacggca acttcaactg gggccgggtt gtcgcccttt tctactttgc cagcaaactg 360
gtgctcaagg ccctgtgcac caaggtgccg gaactgatca gaaccatcat gggctggaca 420
ttggacttcc tccgggagcg gctgttgggc tggatccaag accagggtgg ttgggacggc 480
ctcctctcct actttgggac gcccacgtgg cagaccgtga ccatctttgt ggcgggagtg 540
ctcaccgcct cgctcaccat ctggaagaag atgggctga 579

<210> 34
<211> 657
<212> DNA
<213> Homo sapiens

<300>
<302> Bax beta
<310> L22474

<400> 34
atggacgggt ccggggagca gcccagaggc gggggccca ccagctctga gcagatcatg 60
aagacagggg ccctttttgct tcagggtttc atccaggatc gagcagggcg aatgggggg 120
gaggcaccg agctggccct ggacccggtg cctcaggatg cgtccaccaa gaagctgagc 180
gagtgtctca agcgcatcgg ggacgaactg gacagtaaca tggagctgca gaggatgatt 240
gccgccgtgg acacagactc cccccgagag gtcttttttcc gagtggcagc tgacatgttt 300
tctgacggca acttcaactg gggccgggtt gtcgcccttt tctactttgc cagcaaactg 360
gtgctcaagg ccctgtgcac caaggtgccg gaactgatca gaaccatcat gggctggaca 420
ttggactttcc tccgggagcg gctgttgggc tggatccaag accagggtgg ttgggtgaga 480
ctcctcaagc ctcctcaccc ccaccaccgc gccctcacca ccgcccctgc cccaccgtcc 540
ctgcccccg ccactcctct gggaccctgg gcctctgga gcaggtcaca gtggtgccct 600
ctccccatct tcagatcatc agatgtggtc tataatgcgt tttccttacg tgtctga 657

<210> 35
<211> 432
<212> DNA
<213> Homo sapiens

<300>
<302> Bax delta
<310> U19599

<400> 35
atggacgggt ccggggagca gcccagaggc gggggccca ccagctctga gcagatcatg 60
aagacagggg ccctttttgct tcaggggatg attgccgccg tggacacaga ctccccccga 120
gaggtctttt tccgagtggc agctgacatg ttttctgacg gcaacttcaa ctggggccgg 180
gttgtcgccc ttttctactt tgccagcaaa ctggtgctca aggccctgtg caccaaggtg 240
ccggaactga tcagaaccat catgggctgg acattggact tcctccggga gcggctgttg 300
ggctggatcc aagaccaggg tggttgggac ggcctcctct cctactttgg gacgcccacg 360
tggcagaccg tgaccatctt tgtggcggga gtgctcaccg cctcgctcac catctggaag 420
aagatgggct ga 432

<210> 36
<211> 495
<212> DNA
<213> Homo sapiens

<300>
<302> Bax epsolin
<310> AF007826

<400> 36
atggacgggt ccggggagca gcccagaggc ggggggccca ccagctctga gcagatcatg 60
aagacagggg ccacttttgct tcagggtttc atccaggatc gagcagggcg aatgggggag 120
gaggcacccg agctggccct ggacccggtg cctcaggatg cgtccaccaa gaagctgagc 180
gagtgtctca agcgcatcgg ggacgaactg gacagtaaca tggagctgca gaggatgatt 240
gccgccgtgg acacagactc cccccgagag gtctttttcc gagtggcagc tgacatgttt 300
tctgacggca acttcaactg gggccgggtt gtcgcccttt tctactttgc cagcaaactg 360
gtgctcaagg ctggcgtgaa atggcgtgat ctgggctcac tgcaacctct gcctcctggg 420
ttcaagcgat tcacctgcct cagcatccca aggagctggg attacaggcc ctgtgcacca 480
aggtgccgga actga 495

<210> 37
<211> 582
<212> DNA
<213> Homo sapiens

<300>
<302> bcl-w
<310> U59747

<400> 37
atggcgaccc cagcctcggc cccagacaca cgggctctgg tggcagactt tgtaggttat 60
aagctgaggc agaagggtta tgtctgtgga gctggccccg gggagggccc agcagctgac 120
ccgctgcacc aagccatgcg ggcagctgga gatgagttcg agacccgctt ccggcgcacc 180
ttctctgatc tggcggctca gctgcatgtg accccaggct cagcccagca acgcttcacc 240
caggtctccg acgaacttct tcaaggggcc cccaactggg gccgccttgt agcctttctt 300
gtctttgggg ctgcactgtg tgctgagagt gtcaacaagg agatggaacc actggtggga 360
caagtgcagg agtggatggt ggcctacctg gagacgcggc tggctgactg gatccacagc 420
agtgggggct gggcggagtt cacagctcta tcaggggacg gggccctgga ggaggcgcgg 480
cgtctgcggg aggggaactg ggcatcagtg aggacagtgc tgacgggggc cgtggcactg 540
ggggccctgg taactgtagg ggcctttttt gctagcaagt ga 582

<210> 38
<211> 2481
<212> DNA
<213> Homo sapiens

<300>
<302> HIF-alpha
<310> U22431

<400> 38
atggagggcg ccggcggcgc gaacgacaag aaaaagataa gttctgaacg tcgaaaagaa 60
aagtctcgag atggcagccag atctcggcga agtaaagaat ctgaagtttt ttatgagctt 120
gctcatcagt tgccacttcc acataatgtg agttctgcatc ttgataaggc ctctgtgatg 180
aggcttacca tcagctattt gcgtgtgagg aaactcttgg atgctggtga tttggatatt 240
gaagatgaca tgaaagcaca gatgaattgc ttttatttga aagccttgga tggttttgtt 300
atggttctca cagatgatgg tgacatgatt tacatttctg atаatgtgaa caaatacatg 360
ggattaactc agtttgaact aactggacac agtgtgtttg attttactca tccatgtgac 420
catgaggaaa tgagagaaat gcttacacac agaaatggcc ttgtgaaaaa gggtaaagaa 480
caaaacacac agcgaagctt ttttctcaga atgaagtgta ccctaactag ccgaggaaga 540
actatgaaca taaagtctgc aacatggaag gtattgcact gcacaggcca cattcacgta 600
tatgatacca acagtaacca acctcagtgt gggtataaga aaccacctat gacctgcttg 660
gtgctgattt gtgaacccat tcctcaccca tcaaatattg aaattccttt agatagcaag 720
actttcctca gtcgacacag cctggatatg aaattttctt attgtgatga aagaattacc 780
gaattgatgg gatatgagcc agaagaactt ttaggccgct caatttatga atattatcat 840
gctttggact ctgatcatct gaccaaaact catcatgata tgtttactaa aggacaagtc 900

accacaggac agtacaggat gcttgccaaa agaggtggat atgtctgggt tgaaactcaa 960
gcaactgtca tatataacac caagaattct caaccacagt gcattgtatg tgtgaattac 1020
gttgtgagtg gtattattca gcacgacttg attttctccc ttcaacaaac agaatgtgtc 1080
cttaaaccgg ttgaatcttc agatatgaaa atgactcagc tattcaccaa agttgaatca 1140
gaagatacaa gtagcctctt tgacaaactt aagaaggaac ctgatgcttt aactttgctg 1200
gccccagccg ctggagacac aatcatatct ttagattttg gcagcaacga cacagaaact 1260
gatgaccagc aacttgagga agtaccatta tataatgatg taatgctccc ctcacccaac 1320
gaaaaattac agaatataaa tttggcaatg tctccattac ccaccgctga aacgccaaag 1380
ccacttcgaa gtagtgctga ccctgcactc aatcaagaag ttgcattaaa attagaacca 1440
aatccagagt cactggaact ttcttttacc atgccccaga ttcaggatca gacacctagt 1500
ccttccgatg gaagcactag acaaagttca cctgagccta atagtcccag tgaatattgt 1560
ttttatgtgg atagtgatat ggtcaatgaa ttcaagttgg aattggtaga aaaacttttt 1620
gctgaagaca cagaagcaaa gaacccattt tctactcagg acacagattt agacttggag 1680
atgttagctc cctatatccc aatggatgat gacttccagt tacgttcctt cgatcagttg 1740
tcaccattag aaagcagttc cgcaagccct gaaagcgcaa gtcctcaaag cacagttaca 1800
gtattccagc agactcaaat acaagaacct actgctaatg ccacccactac cactgccacc 1860
actgatgaat taaaaacagt gacaaaagac cgtatggaag acattaaaat attgattgca 1920
tctccatctc ctacccacat acataaagaa actactagtg ccacatcatc accatataga 1980
gatactcaaa gtcggacagc ctcaccaaac agagcaggaa aaggagtcat agaacagaca 2040
gaaaaatctc atccaagaag ccctaacgtg ttatctgtcg ctttgagtca aagaactaca 2100
gttcctgagg aagaactaaa tccaaagata ctagctttgc agaatgctca gagaaagcga 2160
aaaatggaac atgatggttc acttttttcaa gcagtaggaa ttggaacatt attacagcag 2220
ccagacgatc atgcagctac tacatcactt tcttggaaac gtgtaaaagg atgcaaatct 2280
agtgaacaga atggaatgga gcaaaagaca attattttaa taccctctga ttagcatgt 2340
agactgctgg ggcaatcaat ggatgaaagt ggattaccac agctgaccag ttatgattgt 2400
gaagttaatg ctcctataca aggcagcaga aacctactgc agggtgaaga attactcaga 2460
gctttggatc aagttaactg a 2481

<210> 39
<211> 481
<212> DNA
<213> Homo sapiens

<300>
<302> ID1
<310> X77956

<400> 39
atgaaagtcg ccagtggcag caccgccacc gccgccgcgg gccccagctg cgcgctgaag 60
gccggcaaga cagcgagcgg tgcgggcgag gtggtgcgct gtctgtctga gcagagcgtg 120
gccatctcgc gctgccgggg cgccggggcg cgcctgcctg ccctgctgga cgagcagcag 180
gtaaacgtgc tgctctacga catgaacggc tgttactcac gcctcaagga gctggtgccc 240
accctgcccc agaaccgcaa ggtgagcaag gtggagattc tccagcacgt catcgactac 300
atcagggacc ttcagttgga gctgaactcg gaatccgaag ttgggacccc cggggccga 360
gggctgccgg tccgggctcc gctcagcacc ctcaacggcg agatcagcgc cctgacggcc 420
gaggcggcat gcgttcctgc ggacgatcgc atcttgtgtc gctgaatggt gaaaaaaaaa 480
a 481

<210> 40
<211> 110
<212> DNA
<213> Homo sapiens

<300>
<302> ID2B
<310> M96843

<400> 40

tgaaagcctt cagtcccgtg aggtccatta ggaaaaacag cctgttggac caccgcctgg 60
gcatctccca gagcaaaacc ccggtggatg acctgatgag cctgctgtaa 110

<210> 41
<211> 486
<212> DNA
<213> Homo sapiens

<300>
<302> ID4
<310> Y07958

<400> 41
atgaaggcgg tgagcccggt gcgcccctcg ggccgcaagg cgccgtcggg ctgcggcggc 60
ggggagctgg cgctgcgctg cctggccgag cacggccaca gcctgggtgg ctccgcagcc 120
gcggcggcgg cggcggcggc agcgcgctgt aaggcggccg aggcggcggc cgacgagccg 180
gcgctgtgcc tgcagtgcga tatgaacgac tgctatagcc gcctgcggag gctggtgccc 240
accatcccgc ccaacaagaa agtcagcaaa gtggagatcc tgcagcacgt tatcgactac 300
atcctggacc tgcagctggc gctggagacg caccccggccc tgctgaggca gccaccaccg 360
cccgcgccgc cacaccaccc ggccgggacc tgtccagccg cgccgccgcg gaccccgctc 420
actgcgctca acaccgaccc ggccggcgcg gtgaacaagc agggcgacag cattctgtgc 480
cgctga 486

<210> 42
<211> 462
<212> DNA
<213> Homo sapiens

<300>
<302> IGF1
<310> NM000618

<400> 42
atgggaaaaa tcagcagtct tccaacccaa ttatttaagt gctgcttttg tgatttcttg 60
aaggtgaaga tgcacaccat gtcctcctcg catcttcttct acctggcgct gtgcctgctc 120
accttcacca gctctgccac ggctggaccg gagacgctct gcggggctga gctggtggat 180
gctcttcagt tcgtgtgtgg agacaggggc ttttatttca acaagcccac agggtatggc 240
tccagcagtc ggagggcgcc tcagacaggc atcgtggatg agtgctgctt ccggagctgt 300
gatctaagga ggctggagat gtattgcgca cccctcaagc ctgccaagtc agctcgctct 360
gtccgtgccc agcgccacac cgacatgccc aagacccaga aggaagtaca tttgaagaac 420
gcaagtagag ggagtgcagg aaacaagaac tacaggatgt ag 462

<210> 43
<211> 591
<212> DNA
<213> Homo sapiens

<300>
<302> PDGFA
<310> NM002607

<400> 43
atgaggacct tggcttgcct gctgctcctc ggctgcggat acctcgccca tgttctggcc 60
gaggaagccg agatcccccg cgaggtgatc gagaggctgg cccgcagtca gatccacagc 120
atccgggacc tccagcgact cctggagata gactccgtag ggagtgagga ttcttctgac 180
accagcctga gagctcacgg ggtccacgcc actaagcatg tgcccgagaa gcggcccctg 240
cccattcgga ggaagagaag catcgaggaa gctgtccccg ctgtctgcaa gaccaggacg 300

gtcatttacg agattcctcg gagtcaggtc gaccccacgt ccgccaactt cctgatctgg 360
cccccgtgcg tggaggtgaa acgctgcacc ggctgctgca acacgagcag tgtcaagtgc 420
cagcccttcc gcgtccacca ccgcagcgtc aaggtggcca aggtggaata cgtcaggaag 480
aagccaaaat taaaagaagt ccaggtgagg ttagaggagc atttggagtg cgcctgcgcg 540
accacaagcc tgaatccgga ttatcgggaa gaggacacgg atgtgaggtg a 591

<210> 44
<211> 528
<212> DNA
<213> Homo sapiens

<300>
<302> PDGFRA
<310> XM003568

<400> 44
atggccaagc ctgaccacgc taccagtgaa gtctacgaga tcatggtgaa atgctggaac 60
agtgagccgg agaagagacc ctccttttac cacctgagtg agattgtgga gaatctgctg 120
cctggacaat ataaaaagag ttatgaaaaa attcacctgg acttcctgaa gagtgaccat 180
cctgctgtgg cacgcatgcg tgtggactca gacaatgcat acattggtgt cacctacaaa 240
aacgaggaag acaagctgaa ggactgggag ggtggttctgg atgagcagag actgagcgct 300
gacagtggct acatcattcc tctgcctgac attgaccctg tccctgagga ggaggacctg 360
ggcaagagga acagacacag ctcgcagacc tctgaagaga gtgccattga gacgggttcc 420
agcagttcca ccttcatcaa gagagaggac gagaccattg aagacatcga catgatggat 480
gacatcggca tagactcttc agacctggtg gaagacagct tcctgtaa 528

<210> 45
<211> 1911
<212> DNA
<213> Homo sapiens

<300>
<302> PDGFRB
<310> XM003790

<400> 45
atgcggcttc cgggtgcgat gccagctctg gccctcaaag gcgagctgct gttgctgtct 60
ctcctgttac ttctggaacc acagatctct cagggcctgg tcgtcacacc cccggggcca 120
gagcttgtcc tcaatgtctc cagcaccttc gttctgacct gctcgggttc agctccggtg 180
gtgtgggaac ggatgtccca ggagccccca caggaaatgg ccaaggccca ggatggcacc 240
ttctccagcg tgctcacact gaccaacctc actgggctag acacgggaga atacttttgc 300
acccacaatg actcccgtgg actggagacc gatgagcgga aacggctcta catctttgtg 360
ccagatccca ccgtgggctt cctccctaat gatgccgagg aactattcat ctttctcacg 420
gaaataactg agatcaccat tccatgccga gtaacagacc cacagctggt ggtgacactg 480
cacgagaaga aaggggacgt tgcactgcct gtcccctatg atcaccaacg tggcttttct 540
ggtatctttg aggacagaag ctacatctgc aaaaccacca ttggggacag ggagggtggat 600
tctgatgcct actatgtcta cagactccag gtgtcatcca tcaacgtctc tgtgaacgca 660
gtgcagactg tggtccgcca gggtgagaac atcaccctca tgtgcattgt gatcgggaat 720
gaggtggtca acttcgagtg gacataccc cgcaaagaaa gtgggcggct ggtggagccg 780
gtgactgact tcctcttgga tatgccttac cacatccgct ccatcctgca catccccagt 840
gccgagttag aagactcggg gacctacacc tgcaatgtga cggagagtgt gaatgaccat 900
caggatgaaa aggccatcaa catcaccgtg gttgagagcg gctacgtgcg gctcctggga 960
gaggtgggca cactacaatt tgctgagctg catcggagcc ggacactgca ggtagtgttc 1020
gaggcctacc caccgcccac tgtcctgtgg ttcaaagaca accgcaccct ggggcgactcc 1080
agcggtggcg aaatcgccct gtccacgcgc aacgtgtcgg agacccggta tgtgtcagag 1140
ctgacactgg ttcgcgtgaa ggtggcagag gctggccact acaccatgcg ggcctttcat 1200
gaggatgctg aggtccagct ctccttccag ctacagatca atgtccctgt ccgagtgctg 1260
gagctaagtg agagccaccc tgacagtggg gaacagacag tccgctgtcg tggccggggc 1320

atgccccagc cgaacatcat ctggtctgcc tgcagagacc tcaaaaggtg tccacgtgag 1380
ctgccgccca cgctgctggg gaacagttcc gaagaggaga gccagctgga gactaacgtg 1440
acgtactggg aggaggagca ggagtttgag gtggtgagca cactgcgtct gcagcacgtg 1500
gatcggccac tgtcggtgcg ctgcacgctg cgcaaccgct tgggccagga cacgcaggag 1560
gtcatcgtgg tgccacactc cttgcccttt aaggtggtgg tgatctcagc catcctggcc 1620
ctggtggtgc tcaccatcat ctccctttatc atcctcatca tgctttggca gaagaagcca 1680
cgttacgaga tccgatggaa ggtgattgag tctgtgagct ctgacggcca tgagtacatc 1740
tacgtggacc ccatgcagct gccctatgac tccacgtggg agctgccgcg ggaccagctt 1800
gtgctgggac gcaccctcgg ctctggggcc tttgggcagg tggtggaggc cacggttcat 1860
ggcctgagcc attttcaagc cccaatgaaa gtggccgtca aaaatgctta a 1911

<210> 46
<211> 1176
<212> DNA
<213> Homo sapiens

<300>
<302> TGFbeta1
<310> NM000660

<400> 46
atgccgccct ccgggctgcg gctgctgccg ctgctgctac cgctgctgtg gctactggtg 60
ctgacgcctg gcccgccggc cgcgggacta tccacctgca agactatcga catggagctg 120
gtgaagcgga agcgcatcga ggccatccgc ggccagatcc tgtccaagct gcggctcgcc 180
agccccccga gccaggggga ggtgccgccc ggccgctgc ccgaggccgt gctcgccctg 240
tacaacagca cccgcgaccg ggtggccggg gagagtgcag aaccggagcc cgagcctgag 300
gccgactact acgccaagga ggtcacccgc gtgctaatgg tggaaaccca caacgaaatc 360
tatgacaagt tcaagcagag tacacacagc atatatatgt tcttcaacac atcagagctc 420
cgagaagcgg tacctgaacc cgtgttgctc tcccgggcag agctgcgtct gtgaggagg 480
ctcaagttaa aagtggagca gcacgtggag ctgtaccaga aatacagcaa caattcctgg 540
cgatacctca gcaaccggct gctggcaccc agcgactcgc cagagtggtt atctttgat 600
gtcaccggag ttgtgcggca gtggttgagc cgtggagggg aaattgaggg ctttcgcctt 660
agcgcccact gctcctgtga cagcagggat aacacactgc aagtggacat caacgggttc 720
actccggcc gccgaggtga cctggccacc attcatggca tgaaccggcc tttcctgctt 780
ctcatggcca cccgctgga gagggcccag catctgcaaa gctcccggca ccgccgagcc 840
ctggacacca actattgctt cagctccacg gagaagaact gctgcgtgcg gcagctgtac 900
attgacttcc gcaaggacct cggctggaag tggatccacg agcccaaggg ctaccatgcc 960
aacttctgcc tcgggccctg cccctacatt tggagcctgg acacgcagta cagcaaggtc 1020
ctggccctgt acaaccagca taacccgggc gcctcggcgg cgccgtgctg cgtgccgcag 1080
gcgctggagc cgctgcccat cgtgtactac gtgggccgca agcccaaggt ggagcagctg 1140
tccaacatga tcgtgcgctc ctgcaagtgc agctga 1176

<210> 47
<211> 1245
<212> DNA
<213> Homo sapiens

<300>
<302> TGFbeta2
<310> NM003238

<400> 47
atgcactact gtgtgctgag cgcttttctg atcctgcatc tggtcacggt cgcgctcagc 60
ctgtctacct gcagcacact cgatatggac cagttcatgc gcaagaggat cgaggcgatc 120
cgcgggcaga tcctgagcaa gctgaagctc accagtcccc cagaagacta tcctgagccc 180
gaggaagtcc cccggaggt gatttccatc tacaacagca ccagggactt gctccaggag 240
aaggcgagcc ggagggcggc cgcctgcgag cgcgagagga gcgacgaaga gtactacgcc 300
aaggaggttt acaaaatага catgccgccc ttcttcccct ccgaaaatgc catcccgccc 360

actttctaca gaccctactt cagaattgtt cgatttgacg tctcagcaat ggagaagaat 420
gcttccaatt tggtgaaagc agagttcaga gtctttcgtt tgcagaaccc aaaagccaga 480
gtgcctgaac aacggattga gctatatcag attctcaagt ccaaagattt aacatctcca 540
acccagcgct acatcgacag caaagttgtg aaaacaagag cagaaggcga atggctctcc 600
ttcgatgtaa ctgatgctgt tcatgaatgg cttcaccata aagacaggaa cctggatttt 660
aaaataagct tacactgtcc ctgctgcact tttgtaccat ctaataatta catcatccca 720
aataaaagtg aagaactaga agcaagattt gcaggtattg atggcacctc cacatatacc 780
agtggtgatc agaaaactat aaagtccact aggaaaaaaa acagtgggaa gaccccacat 840
ctcctgctaa tgttattgcc ctcctacaga cttgagtcac aacagaccaa ccggcggaag 900
aagcgtgctt tggatgcggc ctattgcttt agaaatgtgc aggataattg ctgcctacgt 960
ccactttaca ttgatttcaa gagggatcta gggtggaaat ggatacacga acccaaaggg 1020
tacaatgcca acttctgtgc tggagcatgc ccgtatttat ggagttcaga ctatcagcac 1080
agcagggtcc tgagcttata taataccata aatccagaag catctgcttc tcttgctgc 1140
gtgtcccaag atttagaacc tctaaccatt ctctactaca ttggcaaaac acccaagatt 1200
gaacagcttt ctaatatgat tgtaaagtct tgcaaatgca gctaa 1245

<210> 48
<211> 1239
<212> DNA
<213> Homo sapiens

<300>
<302> TGFbeta3
<310> XM007417

<400> 48
atgaagatgc acttgcaaag ggctctggtg gtcctggccc tgctgaactt tgccacggtc 60
agcctctctc tgtccacttg caccaccttg gacttcggcc acatcaagaa gaagagggtg 120
gaagccatta ggggacagat cttgagcaag ctcaggctca ccagccccc tgagccaacg 180
gtgatgaccc acgtccccta tcaggtcctg gcccttaca acagcacccg ggagctgctg 240
gaggagatgc atggggagag ggaggaaggc tgcacccagg aaaacaccga gtcggaatac 300
tatgccaaag aaatccataa attcgacatg atccaggggc tggcggagca caacgaactg 360
gctgtctgcc ctaaaggaat tacctccaag gttttcggct tcaatgtgtc ctcagtggag 420
aaaaatagaa ccaacctatt ccgagcagaa ttccgggtct tgcgggtgcc caaccccagc 480
tctaagcgga atgagcagag gatcgagctc ttccagatcc ttcggccaga tgagcacatt 540
gccaaacagc gctatatcgg tggcaagaat ctgcccacac ggggcactgc cgagtggctg 600
tcctttgatg tcactgacac tgtgcgtgag tggctgttga gaagagagtc caacttaggt 660
ctagaaatca gcattcactg tccatgtcac acctttcagc ccaatggaga tatcctggaa 720
aacatttcacg aggtgatgga aatcaaattc aaaggcgtgg acaatgagga tgaccatggc 780
cgtggagatc tggggcgcct caagaagcag aaggatcacc acaaccctca tctaatcctc 840
atgatgattc ccccacaccg gctcgacaac ccgggccagg ggggtcagag gaagaagcgg 900
gctttggaca ccaattactg cttccgcaac ttggaggaga actgctgtgt gcgccccctc 960
tacattgact tccgacagga tctgggctgg aagtgggtcc atgaacctaa gggctactat 1020
gccaacttct gctcaggccc ttgcccatac ctccgcagtg cagacacaac ccacagcacg 1080
gtgctgggac tgtacaacac catcctgtac tatgttggga ggaccccaa agtggagcag 1200
ctctccaaca tggtggtgaa gtcttgtaaa tgtagctga 1239

<210> 49
<211> 1704
<212> DNA
<213> Homo sapiens

<300>
<302> TGFbetaR2
<310> XM003094

<400> 49

atgggtcggg ggctgctcag gggcctgtgg ccgctgcaca tcgtcctgtg gacgcgtatc 60
gccagcacga tcccaccgca cgttcagaag tcggttaata acgacatgat agtcactgac 120
aacaacggtg cagtcaagtt tccacaactg tgtaaatttt gtgatgtgag atttttccacc 180
tgtgacaacc agaaatcctg catgagcaac tgcagcatca cctccatctg tgagaagcca 240
caggaagtct gtgtggctgt atggagaaag aatgacgaga acataaacact agagacagtt 300
tgccatgacc ccaagctccc ctaccatgac tttatttctgg aagatgctgc ttctccaaag 360
tgcattatga aggaaaaaaa aaagcctggt gagacttttct tcatgtgttc ctgtagctct 420
gatgagtgca atgacaacat catcttctca gaagaatata acaccagcaa tcctgacttg 480
ttgctagtca tatttcaagt gacaggcatc agcctcctgc caccactggg agttgccata 540
tctgtcatca tcatctttcta ctgctaccgc gttaaccggc agcagaagct gagttcaacc 600
tgggaaaccg gcaagacgcg gaagctcatg gagttcagcg agcactgtgc catcatcctg 660
gaagatgacc gctctgacat cagctccacg tgtgccaaca acatcaacca caacacagag 720
ctgctgccca ttgagctgga caccctggtg gggaaaggtc gctttgctga ggtctataag 780
gccaagctga agcagaacac ttcagagcag tttgagacag tggcagtcaa gatcttttccc 840
tatgaggagt atgcctcttg gaagacagag aaggacatct tctcagacat caatctgaag 900
catgagaaca tactccagtt cctgacggct gaggagcgga agacggagtt ggggaaacaa 960
tactggctga tcaccgcctt ccacgccaag ggcaacctac aggagtacct gacgcggcat 1020
gtcatcagct gggaggacct gcgcaagctg ggcagctccc tcgcccgggg gattgctcac 1080
ctccacagtg atcacactcc atgtgggagg cccaagatgc ccatcgtgca cagggacctc 1140
aagagctcca atatcctcgt gaagaacgac ctaacctgct gcctgtgtga ctttgggctt 1200
tccctgcgtc tggaccctac tctgtctgtg gatgacctgg ctaacagtgg gcaggtggga 1260
actgcaagat acatggctcc agaagtccta gaatccagga tgaatttgga gaatgttgag 1320
tccttcaagc agaccgatgt ctactccatg gctctggtgc tctgggaaat gacatctcgc 1380
tgtaatgcag tgggagaagt aaaagattat gagcctccat ttggttccaa ggtgcgggag 1440
cacccctgtg tcgaaagcat gaaggacaac gtgttgagag atcgagggcg accagaaatt 1500
cccagctttct ggctcaacca ccagggcatc cagatggtgt gtgagacgtt gactgagtgc 1560
tgggaccacg acccagaggc ccgtctcaca gcccagtgtg tggcagaacg cttcagtgag 1620
ctggagcatc tggacaggct ctcggggagg agctgctcgg aggagaagat tcctgaagac 1680
ggctccctaa acactaccaa atag 1704

<210> 50
<211> 609
<212> DNA
<213> Homo sapiens

<300>
<302> TGFbeta3
<310> XM001924

<400> 50
atgtctcatt acaccattat tgagaatatt tgtcctaaag atgaatctgt gaaattctac 60
agtcccaaga gagtgcactt tcctatcccg caagctgaca tggataagaa gcgattcagc 120
tttgtcttca agcctgtctt caacacctca ctgctctttc tacagtgtga gctgacgctg 180
tgtacgaaga tggagaagca cccccagaag ttgcctaagt gtgtgcctcc tgacgaagcc 240
tgcacctcgc tggacgcctc gatcatctgg gccatgatgc agaatcaaga gacgttcact 300
aagccccttg ctgtgatcca ccatgaagca gaatctaaag aaaaaggtcc aagcatgaag 360
gaaccaaatc caatttctcc accaattttc catggtctgg acaccctaac cgtgatgggc 420
attgcgtttg cagcctttgt gatcggagca ctcctgacgg gggccttgtg gtacatctat 480
tctcacacag gggagacagc aggaaggcag caagtcccca cctccccgcc agcctcggaa 540
aacagcagtg ctgcccacag catcggcagc acgcagagca cgccttgctc cagcagcagc 600
acggcctag 609

<210> 51
<211> 3633
<212> DNA
<213> Homo sapiens

<300>

<302> EGFR
<310> X00588

<400> 51
atgcgaccct ccgggacggc cggggcagcg ctcctggcgc tgctggctgc gctctgcccg 60
gcgagtcggg ctctggagga aaagaaagtt tgccaaggca cgagtaacaa gctcacgcag 120
ttgggcactt ttgaagatca ttttctcagc ctccagagga tgttcaataa ctgtgaggtg 180
gtcttggga atttggaaat tacctatgtg cagaggaatt atgatcttta cttcttaaag 240
accatccagg aggtggctgg ttatgtcctc attgccctca acacagtgga gcgaattcct 300
ttggaaaacc tgcagatcat cagaggaaat atgtactacg aaaattccta tgccttagca 360
gtcttatcta actatgatgc aaataaaacc ggactgaagg agctgcccat gagaaattta 420
caggaaatcc tgcatggcgc cgtgcggttc agcaacaacc ctgccctgtg caacgtggag 480
agcatccagt ggcgggacat agtcagcagt gacttttcta gcaacatgtc gatggacttc 540
cagaaccacc tgggcagctg ccaaaagtgt gatccaagct gtcccaatgg gagctgctgg 600
ggtgcaggag aggagaactg ccagaaactg accaaaatca tctgtgccca gcagtgctcc 660
gggcgctgcc gtggcaagtc ccccagtgac tgctgccaca accagtgtgc tgcaggctgc 720
acaggccccc gggagagcga ctgcctggtc tgccgcaaat tccgagacga agccacgtgc 780
aaggacacct gcccccact catgctctac aaccccacca cgtaccagat ggatgtgaac 840
cccgagggca aatacagctt tggtgccacc tgcgtgaaga agtgtccccg taattatgtg 900
gtgacagatc acggctcgtg cgtccgagcc tgtgggggcg acagctatga gatggaggaa 960
gacggcgtcc gcaagtgtaa gaagtgcgaa gggccttgcc gcaaagtgtg taacggaata 1020
ggtattggtg aatttaaaga ctcactctcc ataaatgcta cgaatattaa acacttcaaa 1080
aactgcacct ccatcagtgg cgatctccac atcctgccgg tggcatttag gggtgactcc 1140
ttcacacata ctcctcctct ggatccacag gaactggata ttctgaaaac cgtaaaggaa 1200
atcacagggt ttttgctgat tcaggcttgg cctgaaaaca ggacggacct ccatgccttt 1260
gagaacctag aaatcatacg cggcaggacc aagcaacatg gtcagttttc ttttgcagtc 1320
gtcagcctga acataacatc cttgggatta cgctccctca aggagataag tgatggagat 1380
gtgatаattt caggaaacaa aaatttgtgc tatgcaaata caataaactg gaaaaaactg 1440
tttgggacct ccggtcagaa aaccaaaatt ataagcaaca gaggtgaaaa cagctgcaag 1500
gccacaggcc aggtctgcca tgccttgtgc tccccgagg gctgctgggg cccgagccc 1560
agggactgcg tctcttgccg gaatgtcagc cgaggcaggg aatgcgtgga caagtgcaag 1620
ctttcggagg gtgagccaag gagtttgtg gagaactctg agtgcataca gtgccacaca 1680
gagtgcctgc ctcaggccat gaacatcacc tgcacaggac ggggaccaga caactgtatc 1740
cagtgtgccc actacattga cggccccac tgcgtcaaga cctgccccgc aggagtcatg 1800
ggagaaaaca acaccctggt ctggaagtac gcagacgccg gccatgtgtg ccacctgtgc 1860
catccaaact gcacctacgg atgcactggg ccagttcttg aaggctgtcc aacgaatgag 1920
cctaagatcc cgtccatcgc cactgggatg gtggggcccc tcctcttgct gctggtggtg 1980
gccctggtgg tcggcctctt catgcgaagg cgccacatcg ttcggaagcg cacgctgcgg 2040
aggctgctgc aggagaggga gcttgtggag cctcttacac ccagtggaga agctcccaac 2100
caagctcttt tgaggatctt gaaggaaact gaattcaaaa agatcaaagt gctgggctcc 2160
ggtgcgttcg gcacggtgta taagggactc tggatcccag aaggtgagaa agttaaaatt 2220
cccgtcgcta tcaaggaatt aagagaagca acatctccga aagccaacaa ggaaatcctc 2280
gatgaagcct acgtgatggc cagcgtggac aaccccacg tgtgccgcct gctgggcatc 2340
tgcctcacct ccacccgtgc actcatcacg cagctcatgc ccttcggctg cctcctggac 2400
tatgtccggg aacacaaaga caatattggc tcccagtacc tgctcaactg gtgtgtgcag 2460
atcgcaaagg gcatgaacta cttggaggac cgtcgcttgg tgcaccgcga cctggcagcc 2520
aggaacgtac tggtgaaaac accgcagcat gtcaagatca cagatttgg gctggccaaa 2580
ctgctgggtg cggaagagaa agaatаccat gcagaaggag gcaaagtgcc tatcaagtgg 2640
atggcattgg aatcaatttt acacagaatc tatacccacc agagtgatgt ctggagctac 2700
ggggtgaccg tttgggagtt gatgaccttt ggatccaagc catatgacgg aatcectgcc 2760
agcgagatct cctccatcct ggagaaagga gaacgcctcc ctcagccacc catatgtacc 2820
atcgatgtct acatgatcat ggtcaagtgc tggatgatag acgcagatag tcgcccaaag 2880
ttccgtgagt tgatcatcga attctccaaa atggcccgag acccccagcg ctaccttgtg 2940
attcaggggg atgaaagaat gcatttgcca agtcctacag actccaactt ctaccgtgcc 3000
ctgatggatg aagaagacat ggacgacgtg gtggatgccg acgagtacct catcccacag 3060
cagggcttct tcagcagccc ctccacgtca cggactcccc tcctgagctc tctgagtgca 3120
accagcaaca attccaccgt ggcttgcatt gatagaaatg ggctgcaaag ctgtcccatc 3180
aagaagaca gcttcttgca gcgatacagc tcagacccca caggcgcctt gactgaggac 3240
agcatagacg acaccttcct cccagtgcct gaatacataa accagtccgt tcccaaaagg 3300
cccgctggct ctgtgcagaa tcctgtctat cacaatcagc ctctgaaccc cgcgcccagc 3360

agagacccac actaccagga cccccacagc actgcagtgg gcaaccccga gtatctcaac 3420
actgtccagc ccacctgtgt caacagcaca ttcgacagcc ctgcccactg ggcccagaaa 3480
ggcagccacc aaattagcct ggacaaccct gactaccagc aggacttctt tcccaaggaa 3540
gccaagccaa atggcatctt taagggctcc acagctgaaa atgcagaata cctaagggtc 3600
gcgccacaaa gcagtgaatt tattggagca tga 3633

<210> 52
<211> 3768
<212> DNA
<213> Homo sapiens

<300>
<302> ERBB2
<310> NM004448

<400> 52
atggagctgg cggcttgtg ccgctggggg ctcctcctcg ccctctttgcc ccccggagcc 60
gcgagcaccc aagtgtgcac cggcacagac atgaagctgc ggctccctgc cagtcccgag 120
acccacctgg acatgctccg ccacctctac cagggctgcc aggtggtgca gggaaacctg 180
gaactcacct acctgcccac caatgccagc ctgtccttcc tgcaggatat ccaggaggtg 240
cagggctacg tgctcatcgc tcacaaccaa gtgaggcagg tcccactgca gaggctgcgg 300
attgtgcgag gcacccagct ctttgaggac aactatgccc tggccgtgct agacaatgga 360
gacccgctga acaataccac ccctgtcaca ggggcctccc caggaggcct gcgggagctg 420
cagctttcgaa gcctcacaga gatctttgaaa ggaggggtct tgatccagcg gaaccccag 480
ctctgctacc aggacacgat tttgtggaag gacatctttcc acaagaacaa ccagctggct 540
ctcacactga tagacaccaa ccgctctcgg gcctgccacc cctgttctcc gatgtgtaag 600
ggctcccgct gctggggaga gagttctgag gattgtcaga gcctgacgcg cactgtctgt 660
gccggtggct gtgcccgctg caaggggcca ctgcccactg actgctgcca tgagcagtgt 720
gctgccggct gcacgggccc caagcactct gactgcctgg cctgcctcca cttcaaccac 780
agtggcatct gtgagctgca ctgcccagcc ctggtcacct acaacacaga cacgtttgag 840
tccatgccca atcccgaggg ccggtataca ttcggcgcca gctgtgtgac tgcctgtccc 900
tacaactacc tttctacgga cgtgggatcc tgcaccctcg tctgcccctt gcacaaccaa 960
gaggtgacag cagaggatgg aacacagcgg tgtgagaagt gcagcaagcc ctgtgcccga 1020
gtgtgctatg gtctgggcat ggagcacttg cgagaggtga gggcagttac cagtgccaat 1080
atccaggagt ttgctggctg caagaagatc tttgggagcc tggcatttct gcggagagc 1140
tttgatgggg acccagcctc caacactgcc ccgctccagc cagagcagct ccaagtgttt 1200
gagacctctgg aagagatcac aggttaccta tacatctcag catggccgga cagcctgcct 1260
gacctcagcg tcttccagaa cctgcaagta atccggggac gaattctgca caatggcgcc 1320
tactcgctga ccctgcaagg gctgggcatc agctggctgg ggctgcgctc actgaggaa 1380
ctgggcagtg gactggccct catccaccat aacacccacc tctgcttcgt gcacacggtg 1440
ccctgggacc agctctttcg gaacccgcac caagctctgc tccacactgc caaccggcca 1500
gaggacgagt gtgtgggcga gggcctggcc tgccaccagc tgtgcgccag agggcactgc 1560
tgggctccag ggcccaccca gtgtgtcaac tgcagccagt tccttcgggg ccaggagtgc 1620
gtggaggaat gccgagtact gcaggggctc ccagggagt atgtgaatgc caggcactgt 1680
ttgccgtgcc accctgagtg tcagccccag aatggctcag tgacctgttt tggaccggag 1740
gctgaccagt gtgtggcctg tgcccactat aaggaccctc ccttctgcgt ggcccgctgc 1800
ccagcggtg tgaaacctga cctctctac atgcccatct ggaagtttcc agatgaggag 1860
ggcgcatgcc agccttgccc catcaactgc acccactcct gtgtggacct ggatgacaag 1920
ggctgccccg ccgagcagag agccagcctt ctgacgtcca tcgtctctgc ggtggttggc 1980
attctgctgg tcgtggtctt gggggtggtc tttgggatcc tcatcaagcg acggcagcag 2040
aagatccgga agtacacgat gcggagactg ctgcaggaaa cggagctggt ggagccgctg 2100
acacctagcg gagcgatgcc caaccaggcg cagatgcgga tcctgaaaga gacggagctg 2160
aggaaggtga agtgcttgg atctggcgct tttggcacag tctacaaggg catctggatc 2220
cctgatgggg agaatgtgaa aattccagtg gccatcaaag tgttgaggga aaacacatcc 2280
cccaaagcca acaaagaaat cttagacgaa gcatacgtga tggctggtgt gggctcccca 2340
tatgtctccc gccttctggg catctgcctg acatccacgg tgcagctggt gacacagctt 2400
atgccctatg gctgcctctt agaccatgtc cgggaaaacc gcggacgcct gggctcccag 2460
gacctgctga actggtgtat gcagattgcc aaggggatga gctacctgga ggatgtgcgg 2520
ctcgtacaca gggacttggc cgctcggaac gtgctggtca agagtcccaa ccatgtcaaa 2580

attacagact tcgggctggc tcggctgctg gacattgacg agacagagta ccatgcagat 2640
ggggggaagg tgcccatcaa gtggatggcg ctggagtcca ttctccgccg gcggttcacc 2700
caccagagtg atgtgtggag ttatggtgtg actgtgtggg agctgatgac ttttggggcc 2760
aaacctacg atgggatccc agcccgggag atccctgacc tgctggaaaa gggggacggg 2820
ctgccccagc ccccatctg caccattgat gtctacatga tcatggtcaa atgttggatg 2880
attgactctg aatgtcggcc aagatttccgg gagtttggtgt ctgaatttctc ccgcatggcc 2940
agggaccccc agcgcttttgt ggtcatccag aatgaggact tgggcccagc cagtcctttg 3000
gacagcacct tctaccgctc actgctggag gacgatgaca tgggggacct ggtggatgct 3060
gaggagtatc tggtacccca gcagggcttc ttctgtccag accctgcccc gggcgctggg 3120
ggcatggtcc accacaggca ccgcagctca tctaccagga gtggcggtgg ggacctgaca 3180
ctagggctgg agcccctctga agaggaggcc cccaggtctc cactggcacc ctccgaaggg 3240
gctggctccg atgtatttga tggtgacctg ggaatggggg cagccaaggg gctgcaaagc 3300
ctccccacac atgaccccag ccctctacag cggtacagtg aggaccccac agtacccctg 3360
ccctctgaga ctgatggcta cgttgccccc ctgacctgca gccccagcc tgaatatgtg 3420
aaccagccag atgttcggcc ccagcccccct tcgccccgag agggccctct gcctgctgcc 3480
cgacctgctg gtgccactct ggaaagggcc aagactctct ccccagggaa gaatgggctc 3540
gtcaaagacg tttttgcctt tgggggtgcc gtggagaacc ccgagtactt gacaccccag 3600
ggaggagctg cccctcagcc ccacccctcct cctgccttca gcccagcctt cgacaacctc 3660
tattactggg accaggaccc accagagcgg gggctccac ccagcacctt caaagggaca 3720
cctacggcag agaacccaga gtacctgggt ctggacgtgc cagtgtga 3768

<210> 53
<211> 1986
<212> DNA
<213> Homo sapiens

<300>
<302> ERBB3
<310> XM006723

<400> 53
atgcacaact tcagtgtttt ttccaatttg acaaccattg gaggcagaag cctctacaac 60
cggggctttct cattgttgat catgaagaac ttgaatgtca catctctggg cttccgatcc 120
ctgaaggaaa ttagtgctgg gcgtatctat ataagtgcca ataggcagct ctgctaccac 180
cactctttga actggaccaa ggtgcttcgg gggcctacgg aagagcgact agacatcaag 240
cataatcggc cgcgcagaga ctgcgtggca gagggcaaag tgtgtgaccc actgtgctcc 300
tctgggggat gctggggccc aggccctggt cagtgcttgt cctgtcgaaa ttagagccga 360
ggagtgtct gtgtgaccca ctgcaacttt ctgaatgggg agcctcgaga atttgcccat 420
gaggccgaat gcttctcctg ccacccggaa tgccaaccca tggagggcac tgccacatgc 480
aatggctcgg gctctgatac ttgtgctcaa tgtgcccatt ttcgagatgg gccccactgt 540
gtgagcagct gccccatgg agtcctaggt gccaaggcc caatctacaa gtaccagat 600
gttcagaatg aatgtcggcc ctgccatgag aactgcaccc aggggtgtaa aggaccagag 660
cttcaagact gtttaggaca aacactggtg ctgatcggca aacccatct gacaatggct 720
ttgacagtga tagcaggatt ggtagtgatt ttcatgatgc tgggcggcac ttttctctac 780
tggcgtgggc gccggattca gaataaaagg gctatgaggc gatacttgga acggggtgag 840
agcatagagc ctctggaccc cagtgagaag gctaacaaag tcttggccag aatcttcaaa 900
gagacagagc taaggaagct taaagtgctt ggctcgggtg tctttggaac tgtgacgaaa 960
ggagtgtgga tccctgaggg tgaatcaatc aagattccag tctgcattaa agtcattgag 1020
gacaagagtg gacggcagag ttttcaagct gtgacagatc atatgctggc cattggcagc 1080
ctggaccatg cccacattgt aaggctgctg ggactatgcc cagggtcatc tctgcagctt 1140
gtcactcaat atttgcctct gggttctctg ctggatcatg tgagacaaca ccgggggtca 1200
ctggggccac agctgctgct caactgggga gtacaaattg ccaagggaat gtactacctt 1260
gaggaacatg gtatggtgca tagaaacctg gctgcccgaa acgtgctact caagtcaccc 1320
agtcaggttc aggtggcaga ttttggtgtg gctgacctgc tgcctcctga tgataagcag 1380
ctgctataca gtgaggccaa gactccaatt aagtggatgg cccttgagag tatccacttt 1440
gggaaatacа cacaccagag tgatgtctgg agctatggtg tgacagttttg ggagttgatg 1500
accttcgggg cagagcccta tgcagggcta cgattggctg aagtaccaga cctgctagag 1560
aaggggagc ggttggcaca gccccagatc tgcacaattg atgtctacat ggtgatggtc 1620
aagtgttgga tgattgatga gaacattcgc ccaacctta aagaactagc caatgagttc 1680

accaggatgg cccgagaccc accacggtat ctggtcataa agagagagag tgggcctgga 1740
atagccccctg ggccagagcc ccatggtctg acaaacaaga agctagagga agtagagctg 1800
gagccagaac tagacctaga cctagacttg gaagcagagg aggacaacct ggcaaccacc 1860
acactgggct ccgccctcag cctaccagtt ggaacactta atcggccacg tgggagccag 1920
agccttttaa gtccatcatc tggatacatg cccatgaacc agggtaatct tggggttctt 1980
ccttag 1986

<210> 54
<211> 1437
<212> DNA
<213> Homo sapiens

<300>
<302> ERBB4
<310> XM002260

<400> 54
atgatgtacc tggaagaaag acgactcgtt catcgggatt tggcagcccg taatgtctta 60
gtgaaatctc caaaccatgt gaaaatcaca gattttgggc tagccagact cttggaagga 120
gatgaaaaag agtacaatgc tgatggagga aagatgccaa ttaaatggat ggctctggag 180
tgtatacatt acaggaaatt cacccatcag agtgacgttt ggagctatgg agttactata 240
tgggaactga tgacctttgg aggaaaaccc tatgatggaa ttccaacgcg agaaatccct 300
gatttattag agaaaggaga acgtttgcct cagcctccca tctgcactat tgacgtttac 360
atggtcatgg tcaaatgttg gatgattgat gctgacagta gacctaaatt taaggaactg 420
gctgctgagt tttcaaggat ggctcgagac cctcaaagat acctagttat tcagggtgat 480
gatcgtatga agcttcccag tccaaatgac agcaagttct ttcagaatct cttggatgaa 540
gaggatttgg aagatatgat ggatgctgag gagtacttgg tccctcaggc tttcaacatc 600
ccacctccca tctatacttc cagagcaaga attgactcga ataggagtga aattggacac 660
agccctcctc ctgcctacac ccccatgtca ggaaaccagt ttgtataccg agatggaggt 720
tttgctgctg aacaaggagt gtctgtgccc tacagagccc caactagcac aattccagaa 780
gctcctgtgg cacagggtgc tactgctgag atttttgatg actcctgctg taatggcacc 840
ctacgcaagc cagtggcacc ccatgtccaa gaggacagta gcacccagag gtacagtgct 900
gaccccaccg tgtttgcccc agaacggagc ccacgaggag agctggatga ggaaggttac 960
atgactccta tgcgagacaa acccaaacaa gaatacctga atccagtgga ggagaaccct 1020
tttgtttctc ggagaaaaaa tggagacctt caagcattgg ataatcccga atatccacaat 1080
gcatccaatg gtccacccaa ggccgaggat gagtatgtga atgagccact gtacctcaac 1140
accttgccca acaccttggg aaaagctgag tacctgaaga acaacatact gtcaatgcca 1200
gagaaggcca agaaagcgtt tgacaaccct gactactgga accacagcct gccacctcgg 1260
agcacccttc agcacccaga ctacctgcag gagtacagca caaaatattt ttataaacag 1320
aatgggcgga tccggcctat tgtggcagag aatcctgaat acctctctga gttctccctg 1380
aagccaggca ctgtgctgcc gcctccacct tacagacacc ggaatactgt ggtgtaa 1437

<210> 55
<211> 627
<212> DNA
<213> Homo sapiens

<300>
<302> FGF10
<310> NM004465

<400> 55
atgtggaaat ggatactgac acattgtgcc tcagcctttc cccacctgcc cggctgctgc 60
tgctgctgct ttttgttgct gttcttggtg tcttccgtcc ctgtcacctg ccaagccctt 120
ggtcaggaca tggtgtcacc agaggccacc aactcttctt cctcctcctt ctcctctcct 180
tccagcgcgg gaaggcatgt gcggagctac aatcaccttc aaggagatgt ccgctggaga 240
aagctattct ctttcaccaa gtactttctc aagattgaga agaacgggaa ggtcagcggg 300
accaagaagg agaactgccc gtacagcatc ctggagataa catcagtaga aatcggagtt 360

gttgccgtca aagccattaa cagcaactat tacttagcca tgaacaagaa ggggaaactc 420
tatggctcaa aagaatttaa caatgactgt aagctgaagg agaggataga ggaaaatgga 480
tacaatacct atgcatcatt taactggcag cataatggga ggcaaatgta tgtggcattg 540
aatggaaaag gagctccaag gagaggacag aaaacacgaa ggaaaaacac ctctgctcac 600
tttcttccaa tggtggtaca ctcatag 627

<210> 56
<211> 679
<212> DNA
<213> Homo sapiens

<300>
<302> FGF11
<310> XM008660

<400> 56
aatggcggcg ctggccagta gcctgatccg gcagaagcgg gaggtccgcg agcccggggg 60
cagccggccg gtgtcggcgc agcggcgcgt gtgtccccgc ggcaccaagt ccctttgcca 120
gaagcagctc ctcatcctgc tgtccaaggt gcgactgtgc gggggcggc ccgcgcggcc 180
ggaccgcggc ccggagcctc agctcaaagg catcgtcacc aaactgttct gccgccaggg 240
tttctacctc caggcgaatc ccgacggaag catccagggc accccagagg ataccagctc 300
cttcacccac ttcaacctga tccctgtggg cctccgtgtg gtcaccatcc agagcgccaa 360
gctgggtcac tacatggcca tgaatgctga gggactgctc tacagttcgc cgcatttcac 420
agctgagtgt cgctttaagg agtgtgtctt tgagaattac tacgtcctgt acgcctctgc 480
tctctaccgc cagcgtcgtt ctggccgggc ctggtacctc ggcctggaca aggagggcca 540
ggtcatgaag ggaaaccgag ttaagaagac caaggcagct gcccactttc tgcccaagct 600
cctggaggtg gccatgtacc aggagccttc tctccacagt gtccccgagg cctccccttc 660
cagtccccct gcccccctga 679

<210> 57
<211> 732
<212> DNA
<213> Homo sapiens

<300>
<302> FGF12
<310> NM021032

<400> 57
atggctgcgg cgatagccag ctccttgatc cggcagaagc ggcaggcgag ggagtccaac 60
agcgaccgag tgtcggcctc caagcgccgc tccagcccca gcaaagacgg gcgctccctg 120
tgcgagaggc acgtcctcgg ggtgttcagc aaagtgcgct tctgcagcgg ccgcaagagg 180
ccggtgaggc ggagaccaga accccagctc aaagggattg tgacaaggtt attcagccag 240
cagggatact tcctgcagat gcacccagat ggtaccattg atgggaccaa ggacgaaaac 300
agcgactaca ctctcttcaa tctaattccc gtgggcctgc gtgtagtggc catccaagga 360
gtgaaggcta gcctctatgt ggccatgaat ggtgaaggct atctctacag ttcagatgtt 420
ttcactccag aatgcaaatt caaggaatct gtgtttgaaa actactatgt gatctattct 480
tccacactgt accgccagca agaatcaggc cgagcttggt ttctgggact caataaagaa 540
ggtcaaatta tgaaggggaa cagagtgaag aaaaccaagc cctcatcaca ttttgtaccg 600
aaacctattg aagtgtgtat gtacagagaa ccatcgctac atgaaattgg agaaaaacaa 660
gggcgttcaa ggaaaagttc tggaacacca accatgaatg gaggcaaagt tgtgaatcaa 720
gattcaacat ag 732

<210> 58
<211> 738
<212> DNA
<213> Homo sapiens

<300>
<302> FGF13
<310> XM010269

<400> 58
atggcggcgg ctatcgccag ctcgctcatc cgtcagaaga ggcaagcccg cgagcgcgag 60
aaatccaacg cctgcaagtg tgtcagcagc cccagcaaag gcaagaccag ctgcgacaaa 120
aacaagttaa atgtcttttc ccgggtcaaa ctcttcggct ccaagaagag gcgcagaaga 180
agaccagagc ctcagcttaa gggtatagtt accaagctat acagccgaca aggctaccac 240
ttgcagctgc aggcggatgg aaccattgat ggcaccaaag atgaggacag cacttacact 300
ctgtttaacc tcatccctgt gggtctgcga gtggtggcta tccaaggagt tcaaaccaag 360
ctgtacttgg caatgaacag tgagggatac ttgtacacct cggaactttt cacacctgag 420
tgcaaattca aagaatcagt gtttgaaaat tattatgtga catattcatc aatgatatac 480
cgtcagcagc agtcaggccg agggtggtat ctgggtctga acaaagaagg agagatcatg 540
aaaggcaacc atgtgaagaa gaacaagcct gcagctcatt ttctgcctaa accactgaaa 600
gtggccatgt acaaggagcc atcactgcac gatctcacgg agttctcccg atctggaagc 660
gggaccccaa ccaagagcag aagtgtctct ggcgtgctga acggaggcaa atccatgagc 720
cacaatgaat caacgtag 738

<210> 59
<211> 624
<212> DNA
<213> Homo sapiens

<300>
<302> FGF16
<310> NM003868

<400> 59
atggcagagg tgggggcgt cttcgcctcc ttggactggg atctacacgg cttctcctcg 60
tctctgggga acgtgccctt agctgactcc ccaggtttcc tgaacgagcg cctgggccaa 120
atcgagggga agctgcagcg tggctcaccc acagacttcg cccacctgaa ggggatcctg 180
cggcgccgcc agctctactg ccgcaccggc ttccacctgg agatcttccc caacggcacg 240
gtgcacggga cccgccacga ccacagccgc ttcggaatcc tggagtttat cagcctggct 300
gtggggctga tcagcatccg gggagtggac tctggcctgt acctaggaat gaatgagcga 360
ggagaactct atgggtcgaa gaaactcaca cgtgaatgtg ttttccggga acagtttgaa 420
gaaaactggt acaacaccta tgcctcaacc ttgtacaaac attcggactc agagagacag 480
tattacgtgg ccctgaacaa agatggctca cccgggagg gatacaggac taaacgacac 540
cagaaattca ctcacttttt acccaggcct gtagatcctt ctaagttgcc ctccatgtcc 600
agagacctct ttcactatag gtaa 624

<210> 60
<211> 651
<212> DNA
<213> Homo sapiens

<300>
<302> FGF17
<310> XM005316

<400> 60
atgggagccg cccgcctgct gcccaacctc actctgtgct tacagctgct gattctctgc 60
tgtcaaactc agggggagaa tcacccgtct cctaatttta accagtacgt gagggaccag 120
ggcgccatga ccgaccagct gagcaggcgg cagatccgcg agtaccaact ctacagcagg 180
accagtggca agcacgtgca ggtcaccggg cgtcgcatct ccgccaccgc cgaggacggc 240
aacaagtttg ccaagctcat agtggagacg gacacgtttg gcagccgggt tcgcatcaaa 300
ggggctgaga gtgagaagta catctgtatg aacaagaggg gcaagctcat cgggaagccc 360

agcgggaaga gcaaagactg cgtgttcacg gagatcgtgc tggagaacaa ctatacggcc 420
ttccagaacg cccggcacga gggctggttc atggccttca cgcggcaggg gcggcccccgc 480
caggcttccc gcagccgcca gaaccagcgc gaggcccact tcatcaagcg cctctaccaa 540
ggccagctgc ccttccccaa ccacgccgag aagcagaagc agttcgagtt tgtgggctcc 600
gcccccaccc gccggaccaa gcgcacacgg cggccccagc ccctcacgta g 651

<210> 61
<211> 624
<212> DNA
<213> Homo sapiens

<300>
<302> FGF18
<310> AF075292

<400> 61
atgtattcag cgccctccgc ctgcacttgc ctgtgtttac acttcctgct gctgtgcttc 60
caggtacagg tgctggttgc cgaggagaac gtggacttcc gcatccacgt ggagaaccag 120
acgcgggctc gggacgatgt gagccgtaag cagctgcggc tgtaccagct ctacagccgg 180
accagtggga aacacatcca ggtcctgggc cgcaggatca gtgcccgcgg cgaggatggg 240
gacaagtatg cccagctcct agtggagaca gacaccttcg gtagtcaagt ccggatcaag 300
ggcaaggaga cggaattcta cctgtgcatg aaccgcaaag gcaagctcgt ggggaagccc 360
gatggcacca gcaaggagtg tgtgttcatc gagaaggttc tggagaacaa ctacacggcc 420
ctgatgtcgg ctaagtactc cggctggtac gtgggcttca ccaagaaggg gcggccgcgg 480
aagggcccca agacccggga gaaccagcag gacgtgcatt tcatgaagcg ctaccccaag 540
gggcagccgg agcttcagaa gcccttcaag tacacgacgg tgaccaagag gtcccgtcgg 600
atccggccca cacaccctgc ctag 624

<210> 62
<211> 651
<212> DNA
<213> Homo sapiens

<300>
<302> FGF19
<310> AF110400

<400> 62
atgcggagcg ggtgtgtggt ggtccacgta tggatcctgg ccggcctctg gctggccgtg 60
gccgggcgcc ccctcgcctt ctcggacgcg gggccccacg tgcactacgg ctggggcgac 120
cccatccgcc tgcggcacct gtacacctcc ggccccccacg ggctctccag ctgcttcctg 180
cgcatccgtg ccgacggcgt cgtggactgc gcgcggggcc agagcgcgca cagtttgctg 240
gagatcaagg cagtcgctct gcggaccgtg gccatcaagg gcgtgcacag cgtgcggtac 300
ctctgcatgg gcgccgacgg caagatgcag gggctgcttc agtactcgga ggaagactgt 360
gctttcgagg aggagatccg cccagatggc tacaatgtgt accgatccga gaagcaccgc 420
ctcccggtct ccctgagcag tgccaaacag cggcagctgt acaagaacag aggcttttctt 480
ccactctctc atttcctgcc catgctgccc atggtcccag aggagcctga ggacctcagg 540
ggccacttgg aatctgacat gttctcttcg ccccctggaga ccgacagcat ggacccattt 600
gggcttgtca ccggactgga ggccgtgagg agtcccagct ttgagaagta a 651

<210> 63
<211> 468
<212> DNA
<213> Homo sapiens

<400> 63
atggctgaag gggaaatcac caccttcaca gccctgaccg agaagtttaa tctgcctcca 60

gggaattaca agaagcccaa actcctctac tgtagcaacg ggggccactt cctgaggatc 120
cttccggatg gcacagtgga tgggacaagg gacaggagcg accagcacat tcagctgcag 180
ctcagtgcgg aaagcgtggg ggaggtgtat ataaagagta ccgagactgg ccagtacttg 240
gccatggaca ccgacgggct tttatacggc tcacagacac caaatgagga atgtttgttc 300
ctggaaaggc tggaggagaa ccattacaac acctatatat ccaagaagca tgcagagaag 360
aattggtttg ttggcctcaa gaagaatggg agctgcaaac gcggtcctcg gactcactat 420
ggccagaaag caatcttgtt tctccccctg ccagtcttct ctgattaa 468

<210> 64
<211> 636
<212> DNA
<213> Homo sapiens

<300>
<302> FGF20
<310> NM019851

<400> 64
atggctccct tagccgaagt cgggggcttt ctgggcggcc tggagggctt gggccagcag 60
gtgggttcgc atttcctgtt gcctcctgcc ggggagcggc cgccgctgct gggcgagcgc 120
aggagcgcgg cggagcggag cgcccgcggc gggccgggag ctgcgcagct ggcgcacctg 180
cacggcatcc tgcgccgccg gcagctctat tgccgcaccg gcttccacct gcagatcctg 240
cccgacggca gcgtgcaggg cacccggcag gaccacagcc tcttcggtat cttggaattc 300
atcagtgtgg cagtgggact ggtcagtatt agaggtgtgg acagtggtct ctatcttgga 360
atgaatgaca aaggagaact ctatggatca gagaaactta cttccgaatg catctttagg 420
gagcagtttg aagagaactg gtataacacc tattcatcta acatatataa acatggagac 480
actggccgca ggtattttgt ggcacttaac aaagacggaa ctccaagaga tggcgccagg 540
tccaagaggc atcagaaatt tacacatttc ttacctagac cagtggatcc agaaagagtt 600
ccagaattgt acaaggacct actgatgtac acttga 636

<210> 65
<211> 630
<212> DNA
<213> Homo sapiens

<300>
<302> FGF21
<310> XM009100

<400> 65
atggactcgg acgagaccgg gttcgagcac tcaggactgt gggtttctgt gctggctggt 60
cttctgctgg gagcctgcca ggcacacccc atccctgact ccagtcctct cctgcaattc 120
gggggccaag tccggcagcg gtacctctac acagatgatg cccagcagac agaagcccac 180
ctggagatca gggaggatgg gacggtgggg ggcgctgctg accagagccc cgaaagtctc 240
ctgcagctga aagccttgaa gccgggagtt attcaaatct tgggagtcaa gacatccagg 300
ttcctgtgcc agcggccaga tggggccctg tatggatcgc tccactttga ccctgaggcc 360
tgcagctttc gggagctgct tcttgaggac ggatacaatg tttaccagtc cgaagcccac 420
ggcctcccgc tgcacctgcc agggaacaag tccccacacc gggaccctgc accccgagga 480
ccagctcgct tcctgccact accaggcctg ccccccgcac tcccggagcc acccggaatc 540
ctggcccccc agccccccga tgtgggctcc tcggaccctc tgagcatggt gggaccttcc 600
cagggccgaa gccccagcta cgcttcctga 630

<210> 66
<211> 513
<212> DNA
<213> Homo sapiens

<300>
<302> FGF22
<310> XM009271

<400> 66
atgcgccgcc gcctgtggct gggcctggcc tggctgctgc tggcgcgggc gccggacgcc 60
gcgggaaccc cgagcgcgtc gcggggaccg cgcagctacc cgcacctgga gggcgacgtg 120
cgctggcggc gcctcttctc ctccactcac ttcttcctgc gcgtggatcc cggcggccgc 180
gtgcagggca cccgctggcg ccacggccag gacagcatcc tggagatccg ctctgtacac 240
gtgggcgtcg tggtcatcaa agcagtgtcc tcaggcttct acgtggccat gaaccgccgg 300
ggccgcctct acgggtcgcg actctacacc gtggactgca ggttccggga gcgcatcgaa 360
gagaacggcc acaacaccta cgcctcacag cgctggcgcc gccgcggcca gcccatgttc 420
ctggcgctgg acaggagggg ggggccccgg ccaggcggcc ggacgcggcg gtaccacctg 480
tccgcccact tcctgcccgt cctggtctcc tga 513

<210> 67
<211> 621
<212> DNA
<213> Homo sapiens

<300>
<302> FGF4
<310> NM002007

<400> 67
atgtcggggc ccgggacggc cgcggtagcg ctgctcccgg cggtcctgct ggccttgctg 60
gcgccctggg cgggccgagg gggcgccgcc gcacccactg cacccaacgg cacgctggag 120
gccgagctgg agcgccgctg ggagagcctg gtggcgctct cgttggcgcg cctgccgggtg 180
gcagcgcagc ccaaggaggc ggccgtccag agcggcgccg gcgactacct gctgggcatc 240
aagcggctgc ggcggctcta ctgcaacgtg ggcatcggct tccacctcca ggcgctcccc 300
gacggccgca tcggcggcgc gcacgcggac acccgcgaca gcctgctgga gctctcgccc 360
gtggagcggg gcgtggtgag catcttcggc gtggccagcc ggttcttcgt ggccatgagc 420
agcaagggca agctctatgg ctcgcccttc ttcaccgatg agtgcacgtt caaggagatt 480
ctccttccca acaactacaa cgcctacgag tcctacaagt accccggcat gttcatcgcc 540
ctgagcaaga atgggaagac caagaagggg aaccgagtgt cgcccaccat gaaggtcacc 600
cacttcctcc ccaggctgtg a 621

<210> 68
<211> 597
<212> DNA
<213> Homo sapiens

<300>
<302> FGF6
<310> NM020996

<400> 68
atgtcccggg gagcaggacg tctgcagggc acgctgtggg ctctcgtctt cctaggcatc 60
ctagtgggca tggtggtgcc ctcgcctgca ggcacccgtg ccaacaacac gctgctggac 120
tcgaggggct ggggcaccct gctgtccagg tctcgcgcgg ggctagctgg agagattgcc 180
ggggtgaact gggaaagtgg ctatttggtg gggatcaagc ggcagcggag gctctactgc 240
aacgtgggca tcggctttca cctccaggtg ctccccgacg gccggatcag cgggacccac 300
gaggagaacc cctacagcct gctggaaatt tccactgtgg agcgaggcgt ggtgagtctc 360
tttggagtga gaagtgccct cttcgttgcc atgaacagta aaggaagatt gtacgcaacg 420
cccagcttcc aagaagaatg caagttcaga gaaaccctcc tgcccaacaa ttacaatgcc 480
tacgagtcag acttgtacca agggacctac attgccctga gcaaatacgg acgggtaaag 540
cggggcagca aggtgtcccc gatcatgact gtcactcatt tccttcccag gatctaa 597

<210> 69
<211> 150
<212> DNA
<213> Homo sapiens

<300>
<302> FGF7
<310> XM007559

<400> 69
atgtctttggc aatgcacttc atacacaatg actaatctat actgtgatga tttgactcaa 60
aaggagaaaa gaaattatgt agttttcaat tctgattcct attcaccttt tgtttatgaa 120
tggaaagctt tgtgcaaaat atacatataa 150

<210> 70
<211> 628
<212> DNA
<213> Homo sapiens

<300>
<302> FGF9
<310> XM007105

<400> 70
gatggctccc ttaggtgaag ttgggaacta tttcggtgtg caggatgcgg taccgtttgg 60
gaatgtgccc gtgttgccgg tggacagccc ggttttgtta agtgaccacc tgggtcagtc 120
cgaagcaggg gggctcccca ggggacccgc agtcacggac ttggatcatt taaaggggat 180
tctcaggcgg aggcagctat actgcaggac tggatttcac ttagaaatct tccccaatgg 240
tactatccag ggaaccagga aagaccacag ccgatttggc attctggaat ttatcagtat 300
agcagtgggc ctggtcagca ttcgaggcgt ggacagtgga ctctacctcg ggatgaatga 360
gaaggggggag ctgtatggat cagaaaaact aacccaagag tgtgtattca gagaacagtt 420
cgaagaaaac tggtataata cgtactcatc aaacctatat aagcacgtgg acactggaag 480
gcgatactat gttgcattaa ataaagatgg gaccccgaga gaagggacta ggactaaacg 540
gcaccagaaa ttcacacatt ttttacctag accagtggac cccgacaaag tacctgaact 600
gtataaggat attctaagcc aaagttga 628

<210> 71
<211> 2469
<212> DNA
<213> Homo sapiens

<300>
<302> FGFR1
<310> NM000604

<400> 71
atgtggagct ggaagtgcct cctcttctgg gctgtgctgg tcacagccac actctgcacc 60
gctaggccgt ccccgacctt gcctgaacaa gcccagccct ggggagcccc tgtggaagtg 120
gagtcctttc tggtccaccc cggtgacctg ctgcagcttc gctgtcggct gcgggacgat 180
gtgcagagca tcaactggct gcgggacggg gtgcagctgg cggaaagcaa ccgcacccgc 240
atcacagggg aggaggtgga ggtgcaggac tccgtgcccg cagactccgg cctctatgct 300
tgcgtaacca gcagccccte gggcagtgac accacctact tctccgtcaa tgtttcagat 360
gctctccccct cctcggagga tgatgatgat gatgatgact cctcttcaga ggagaaagaa 420
acagataaca ccaaaccaaa ccgtatgccc gtagctccat attggacatc cccagaaaag 480
atggaaaaga aattgcatgc agtgccggct gccaagacag tgaagttcaa atgcccttcc 540
agtgggaccc caaaccccac actgcgctgg ttgaaaaatg gcaaagaatt caaacctgac 600
cacagaattg gaggctacaa ggtccgttat gccacctgga gcatcataat ggactctgtg 660

gtgccctctg acaagggcaa ctcacctgc attgtggaga atgagtacgg cagcatcaac 720
cacacatacc agctggatgt cgtggagcgg tcccctcacc ggcccatcct gcaagcaggg 780
ttgcccgcca acaaaacagt ggccctgggt agcaacgtgg agttcatgtg taaggtgtac 840
agtgacccgc agccgcacat ccagtggcta aagcacatcg aggtgaatgg gagcaagatt 900
ggcccagaca acctgcctta tgtccagatc ttgaagactg ctggagttaa taccaccgac 960
aaagagatgg aggtgcttca cttaagaaat gtctcctttg aggacgcagg ggagtatacg 1020
tgcttggcgg gtaactctat cggactctcc catcactctg catggttgac cgttctggaa 1080
gccctggaag agaggccggc agtgatgacc tcgccctgt acctgagagt catcatctat 1140
tgcacagggg ccttcctcat ctcctgcatg gtggggtcgg tcatcgtcta caagatgaag 1200
agtggtacca agaagagtga cttccacagc cagatggctg tgcacaagct ggccaagagc 1260
atccctctgc gcagacaggt aacagtgtct gctgactcca gtgcatccat gaactctggg 1320
gttcttctgg ttcggccatc acggctctcc tccagtggga ctcccatgct agcagggggtc 1380
tctgagtatg agcttcccga agaccctcgc tgggagctgc ctcgggacag actggtctta 1440
ggcaaacccc tgggagaggg ctgctttggg caggtggtgt tggcagaggc tatcgggctg 1500
gacaaggaca aacccaaccg tgtgaccaaa gtggctgtga agatgttgaa gtcggacgca 1560
acagagaaag acttgtcaga cctgatctca gaaatggaga tgatgaagat gatcgggaag 1620
cataagaata tcatcaacct gctgggggcc tgcacgcagg atggtccctt gtatgtcatc 1680
gtggagtatg cctccaaggg caacctgcgg gagtacctgc aggcccggag gcccccaggg 1740
ctggaatact gctacaaccc cagccacaac ccagaggagc agctctcctc caaggacctg 1800
gtgtcctgcg cctaccaggt ggcccgaggc atggagtatc tggcctccaa gaagtgcata 1860
caccgagacc tggcagccag gaatgtcctg gtgacagagg acaatgtgat gaagatagca 1920
gactttggcc tcgcacggga cattcaccac atcgactact ataaaaagac aaccaacggc 1980
cgactgcctg tgaagtggat ggcacccgag gcattatttg accggatcta cacccaccag 2040
agtgatgtgt ggtctttcgg ggtgtcctcg tgggagatct tcactctggg cggctcccca 2100
taccccggtg tgcctgtgga ggaacttttc aagctgctga aggagggtca ccgcatggac 2160
aagcccagta actgcaccaa cgagctgtac atgatgatgc gggactgctg gcatgcagtg 2220
ccctcacaga gacccacctt caagcagctg gtggaagacc tggaccgcat cgtggccttg 2280
acctccaacc aggagtacct ggacctgtcc atgccctgg accagtactc ccccagcttt 2340
cccgacaccc ggagctctac gtgctcctca ggggaggatt ccgtcttctc tcatgagccg 2400
ctgcccgagg agccctgcct gccccgacac ccagcccagc ttgccaatgg cggactcaaa 2460
cgccgctga 2469

<210> 72
<211> 2409
<212> DNA
<213> Homo sapiens

<300>
<302> FGFR4
<310> XM003910

<400> 72
atgcggctgc tgctggccct gttgggggtc ctgctgagtg tgcctgggcc tccagtcttg 60
tccctggagg cctctgagga agtggagctt gagccctgcc tggctcccag cctggagcag 120
caagagcagg agctgacagt agcccttggg cagcctgtgc ggctgtgctg tgggcgggct 180
gagcgtggtg gccactggta caaggagggc agtcgcctgg cacctgctgg ccgtgtacgg 240
ggctggaggg gccgcctaga gattgccagc ttcctacctg aggatgctgg ccgctacctc 300
tgcctggcac gaggctccat gatcgtcctg cagaatctca ccttgattac aggtgactcc 360
ttgacctcca gcaacgatga tgaggacccc aagtcccata gggacctctc gaataggcac 420
agttaccccc agcaagcacc ctactggaca caccccagc gcatggagaa gaaactgcat 480
gcagtacctg cggggaacac cgtcaagttc cgctgtccag ctgcaggcaa ccccagcgcc 540
accatccggt ggcttaagga tggacaggcc tttcatgggg agaaccgcat tggaggcatt 600
cggctgcgcc atcagcactg gagtctcgtg atggagagcg tggtgccctc ggaccgcggc 660
acatacacct gcctggtaga gaacgctgtg ggcagcatcc gttataacta ccctgctagat 720
gtgctggagc ggtccccgca ccggcccatc ctgcaggccg ggctcccggc caacaccaca 780
gccgtggtgg gcagcgacgt ggagctgctg tgcaaggtgt acagcgatgc ccagccccac 840
atccagtggc tgaagcacat cgtcatcaac ggcagcagct tcggagccga cggtttcccc 900
tatgtgcaag tcctaaagac tgcagacatc aatagctcag aggtggaggt cctgtacctg 960
cggaacgtgt cagccgagga cgcaggcgag tacacctgcc tcgcaggcaa ttccatcggc 1020

ctctcctacc agtctgcctg gctcacggtg ctgccagagg aggaccccac atggaccgca 1080
gcagcgcccg aggccaggta tacggacatc atcctgtacg cgtcgggctc cctggccttg 1140
gctgtgctcc tgctgctggc caggctgtat cgagggcagg cgctccacgg ccggcacccc 1200
cgcccgcccg ccactgtgca gaagctctcc cgcttccctc tggcccgaca gttctccctg 1260
gagtcaggct ctttccggca gtcaagctca tccctggtac gaggcgtgcg tctctcctcc 1320
agcggcccca ccttgctcgc cggcctcgtg agtctagatc tacctctcga ccctactatg 1380
gagttccccc gggacaggct ggtgcttggg aagcccctag gcgagggctg ctttggccag 1440
gtagtacgtg cagaggcctt tggcatggac cctgcccggc cgtaccaagc cagcactgtg 1500
gccgtcaaga tgctcaaaga caacgcctct gacaaggacc tggccgacct ggtctcggag 1560
atggaggtga tgaagctgat cggccgacac aagaacatca tcaacctgct tggtgtctgc 1620
acccaggaag ggcccctgta cgtgatcgtg gagtgcgccg ccaagggaaa cctgccgggag 1680
ttcctgcggg cccggcgccc cccaggcccc gacctcagcc ccgacggtcc tcggagcagt 1740
gaggggccgc tctccttccc agtcctggtc tcctgcgcct accaggtggc ccgaggcatg 1800
cagtatctgg agtcccggaa gtgtatccac cgggacctgg ctgcccgcaa tgtgctggtg 1860
actgaggaca atgtgatgaa gattgctgac tttgggctgg cccgcggcgt ccaccacatt 1920
gactactata agaaaaccag caacggccgc ctgcctgtga agtggatggc gcccgaggcc 1980
ttgtttgacc gggtgtacac acaccagagt gacgtgtggt cttttgggat cctgctatgg 2040
gagatcttca ccctcggggg ctccccgtat cctggcatcc cggtggagga gctgttctcg 2100
ctgctgcggg agggacatcg gatggaccga ccccacact gccccccaga gctgtacggg 2160
ctgatgcgtg agtgctggca cgcagcgccc tcccagaggc ctaccttcaa gcagctggtg 2220
gaggcgctgg acaaggtcct gctggccgtc tctgaggagt acctcgacct ccgcctgacc 2280
ttcggaccct attccccctc tggtggggac gccagcagca cctgctcctc cagccgattct 2340
gtcttcagcc acgacccccct gccattggga tccagctcct tccccttcgg gtctggggtg 2400
cagacatga 2409

<210> 73
<211> 1695
<212> DNA
<213> Homo sapiens

<300>
<302> MT2MMP
<310> D86331

<400> 73
atgaagcggc cccgctgtgg ggtgccagac cagttcgggg tacgagtgaa agccaacctg 60
cggcggcgtc ggaagcgcta cgccctcacc gggaggaagt ggaacaacca ccatctgacc 120
tttagcatcc agaactacac ggagaagttg ggctggtacc actcgatgga ggcggtgcgc 180
agggccttcc gcgtgtggga gcaggccacg ccctggtct tccaggaggt gccctatgag 240
gacatccggc tgcggcgaca gaaggaggcc gacatcatgg tactctttgc ctctggcttc 300
cacggcgaca gctcgccgtt tgatggcacc ggtggctttc tggcccacgc ctatttccct 360
ggccccggcc taggcgggga cacccatttt gacgcagatg agccctggac cttctccagc 420
actgacctgc atggaaacaa cctcttcctg gtggcagtgc atgagctggg ccacgcgctg 480
gggctggagc actccagcaa ccccaatgcc atcatggcgc cgttctacca gtggaaggac 540
gttgacaact tcaagctgcc cgaggacgat ctccgtggca tccagcagct ctacggagtacc 600
ccagacggtc agccacagcc tacccagcct ctccccactg tgacgccacg gcggccaggc 660
cggcctgacc accggccgcc ccggcctccc cagccaccac ccccaggtgg gaagccagag 720
cggccccaa agccgggccc cccagtccag ccccgagcca cagagcggcc cgaccagtat 780
ggccccaaca tctgcgacgg ggactttgac acagtggcca tgcttcgcgg ggagatgttc 840
gtgttcaagg gccgctggtt ctggcgagtc cggcacaacc gcgtcctgga caactatccc 900
atgcccatcg ggcacttctg gcgtggttctg cccggtgaca tcagtgctgc ctacgagcgc 960
caagacggtc gttttgtctt tttcaaaggt gaccgctact ggctctttcg agaagcgaac 1020
ctggagcccg gctacccaca gccgctgacc agctatggcc tgggcatccc ctatgaccgc 1080
attgacagcg ccatctggtg ggagccccca ggccacacct tcttcttcca agaggacagg 1140
tactggcgct tcaacgagga gacacagcgt ggagaccctg ggtaccccaa gcccatcagt 1200
gtctggcagg ggatccctgc ctcccctaaa ggggccttcc tgagcaatga cgcagcctac 1260
acctacttct acaaggggcac caaatactgg aaattcgaca atgagcgcct gcggatggag 1320
cccggctacc ccaagtccat cctgcgggac ttcatgggct gccaggagca cgtggagcca 1380
ggccccgat ggccgacgt ggccccggccg cccttcaacc cccacggggg tgcagagccc 1440

ggggcggaca gcgcagaggg cgacgtgggg gatggggatg gggactttgg ggccggggtc 1500
aacaaggaca ggggcagccg cgtggtggtg cagatggagg agggtggcacg gacggtgaac 1560
gtggtgatgg tgctggtgcc actgctgctg ctgctctgcg tcctgggcct cacctacgcg 1620
ctggtgcaga tgcagcgcaa gggtgcgcca cgtgtcctgc tttactgcaa gcgctcgctg 1680
caggagtggg tctga 1695

<210> 74
<211> 1824
<212> DNA
<213> Homo sapiens

<300>
<302> MT3MMP
<310> D85511

<400> 74
atgatcttac tcacattcag cactggaaga cggttggatt tcgtgcatca ttcgggggtg 60
tttttcttgc aaaccttgct ttggatttta tgtgctacag tctgcggaac ggagcagtat 120
ttcaatgtgg aggtttggtt acaaaagtac ggctaccttc caccgactga ccccagaatg 180
tcagtgctgc gctctgcaga gaccatgcag tctgccctag ctgccatgca gcagttctat 240
ggcattaaca tgacaggaaa agtggacaga aacacaattg actggatgaa gaagccccga 300
tgcggtgtac ctgaccagac aagaggtagc tccaaatttc atattcgtcg aaagcgatat 360
gcattgacag gacagaaatg gcagcacaag cacatcactt acagtataaa gaacgtaact 420
ccaaaagtag gagaccctga gactcgtaaa gctattcgcc gtgcctttga tgtgtggcag 480
aatgtaactc ctctgacatt tgaagaagtt ccctacagtg aattagaaaa tggcaaacgt 540
gatgtggata taaccattat ttttgcatct ggtttccatg gggacagctc tccctttgat 600
ggagagggag gatttttggc acatgcctac ttccctggac caggaattgg aggagatacc 660
cattttgact cagatgagcc atggacacta ggaaatccta atcatgatgg aaatgactta 720
tttcttgtag cagtccatga actgggacat gctctgggat tggagcattc caatgacccc 780
actgccatca tggctccatt ttaccagtac atggaaacag acaacttcaa actacctaat 840
gatgatttac agggcatcca gaagatatat ggtccacctg acaagattcc tccacctaca 900
agacctctac cgacagtgcc cccacaccgc tctattcctc cggctgaccc aaggaaaaat 960
gacaggccaa aacctcctcg gcctccaacc ggcagaccct cctatcccgg agccaaaccc 1020
aacatctgtg atgggaactt taacactcta gctattcttc gtcgtgagat gtttgttttc 1080
aaggaccagt ggttttggcg agtgagaaac aacagggtga tggatggata cccaatgcaa 1140
attacttact tctggcgggg cttgcctcct agtatcgatg cagtttatga aaatagcgac 1200
gggaatttg tgttctttaa aggtaacaaa tattgggtgt tcaaggatac aactcttcaa 1260
cctggttacc ctcatgactt gataaccctt ggaagtggaa ttccccctca tggtattgat 1320
tcagccattt ggtgggagga cgtcgggaaa acctatttct tcaagggaga cagatattgg 1380
agatatagtg aagaaatgaa aacaatggac cctggctatc ccaagccaat cacagtctgg 1440
aaagggatcc ctgaatctcc tcagggagca tttgtacaca aagaaaatgg ctttacgtat 1500
ttctacaaag gaaaggagta ttggaaattc aacaaccaga tactcaaggt agaacctgga 1560
tatccaagat ccatcctcaa ggatttatg ggctgtgatg gaccaacaga cagagttaaa 1620
gaaggacaca gcccaccaga tgatgtagac attgtcatca aactggacaa cacagccagc 1680
actgtgaaag ccatagctat tgtcattccc tgcatcttgg ccttatgcct ccttgtattg 1740
gtttacactg tgttccagtt caagaggaaa ggaacacccc gccacatact gtactgtaaa 1800
cgctctatgc aagagtgggt gtga 1824

<210> 75
<211> 1818
<212> DNA
<213> Homo sapiens

<300>
<302> MT4MMP
<310> AB021225

<400> 75

```
atgcggcgcc gcgcagcccg gggacccggc ccgccgcccc cagggcccgg actctcgcgg 60
ctgccgctgc tgccgctgcc gctgctgctg ctgctggcgc tggggacccg cgggggctgc 120
gccgcgccgg aacccgcgcg gcgcgccgag gacctcagcc tgggagtgga gtggctaagc 180
aggttcggtt acctgccccc ggctgacccc acaacagggc agctgccagc gaagaggag 240
ctgtctaagg ccatcacagc catgcagcag tttggtggcc tggaggccac cggcatcctg 300
gacgaggcca ccctggccct gatgaaaacc ccacgctgct ccctgccaga cctccctgtc 360
ctgacccagg ctcgcaggag acgccaggct ccagccccca ccaagtggaa caagaggaac 420
ctgtcgtgga gggtccggac gttcccacgg gactcaccac tggggcacga cacggtgcgt 480
gcactcatgt actacgccct caaggttctgg agcgacattg cgccccctgaa cttccacgag 540
gtggcgggca gcaccgccga catccagatc gacttctcca aggccgacca taacgacggc 600
taccccttcg acgccggcgg gcaccgtgcc cacgcctttct tccccggcca ccaccacacc 660
gccgggtaca cccactttaa cgatgacgag gcctggacct tccgctcctc ggatgcccac 720
gggatggacc tgtttgcagt ggctgtccac gagtttggcc acgccattgg gttaagccat 780
gtggccgctg cacactccat catgcggccg tactaccagg gcccggtggg tgacccgctg 840
cgctacgggc tcccctacga ggacaaggtg cgcgtctggc agctgtacgg tgtgcgggag 900
tctgtgtctc ccacggcgca gcccgaggag cctccccctgc tgccggagcc cccagacaac 960
cggtccagcg cccgcccag gaaggacgtg ccccacagat gcagcactca ctttgacgcg 1020
gtggcccaga tccgggggtga agctttcttc ttcaaaggca agtacttctg gcggctgacg 1080
cgggacccgc acctggtgtc cctgcagccg gcacagatgc accgcttctg gcggggcctg 1140
ccgctgcacc tggacagcgt ggacgccgtg tacgagcgca ccagcgacca caagatcgtc 1200
ttcttttaaag gagacaggta ctgggtgttc aaggacaata acgtagagga aggatacccg 1260
cgcccgtct ccgacttcag cctcccgcct ggcggcatcg acgctgcctt ctcctgggcc 1320
cacaatgaca ggacttattt ctttaaggac cagctgtact ggcgctacga tgaccacacg 1380
aggcacatgg acccccggcta cccccccag agccccctgt ggaggggtgt ccccagcacg 1440
ctggacgacg ccatgcgctg gtccgacggt gcctcctact tcttccgtgg ccaggagtac 1500
tggaaagtgc tggatggcga gctggaggtg gcacccgggt acccacagtc cacggcccgg 1560
gactggctgg tgtgtggaga ctcacaggcc gatggatctg tggctgcggg cgtggacgcg 1620
gcagaggggc cccgcgcccc tccaggacaa catgaccaga gccgctcgga ggacggttac 1680
gaggtctgct catgcacctc tggggcatcc tctcccccgg gggccccagg cccactggtg 1740
gctgccacca tgctgctgct gctgccgcca ctgtcaccag gcgccctgtg gacagcggcc 1800
caggccctga cgctatga                                              1818
```

<210> 76
<211> 1938
<212> DNA
<213> Homo sapiens

<300>
<302> MT5MMP
<310> AB021227

<400> 76

```
atgccgagga gccgggggcgg ccgcgccgcg ccggggccgc cgccgccgcc gccgccgccg 60
ggccaggccc cgcgctggag ccgctggcgg gtccctgggc ggctgctgct gctgctgctg 120
cccgcgctct gctgcctccc gggcgccgcg cgggcggcgg cggcggcggc ggcggcaggg 180
aaccgggcag cggtggcggt ggcggtggcg cgggcggacg aggcggaggc gcccttcgcc 240
gggcagaact ggttaaagtc ctatggctat ctgcttccct atgactcacg ggcatctgcg 300
ctgcactcag cgaaggcctt gcagtcggca gtctccacta tgcagcagtt ttacggggatc 360
ccggtcaccg gtgtgttgga tcagacaacg atcgagtgga tgaagaaacc cgagatgtggt 420
gtccctgatc accccactt aagccgtagg cggagaaaca agcgctatgc cctgactgga 480
cagaagtgga ggcaaaaaca catcacctac agcattcaca actatacccc aaaagtgggt 540
gagctagaca cgcggaaagc tattcgccag gctttcgatg tgtggcagaa ggtgacccca 600
ctgaccttg aagaggtgcc ataccatgag atcaaaagtg accggaagga gtcagacatc 660
atgatctttt ttgcttctgg tttccatggc gacagctccc catttgatgg agaaggggga 720
ttcctggccc atgcctactt ccctggccca gggattggag gagacaccca ctttgactcc 780
gatgagccat ggacgctagg aaacgccaac catgacggga acgacctctt cctggtggct 840
gtgcatgagc tgggccacgc gctgggactg gagcactcca gcgacccccag cgccatcatg 900
gcgccctct accagtacat ggagacgcac aacttcaagc tgcccccagga cgatctccag 960
ggcatccaga agatctatgg acccccagcc gagcctctgg agcccacaag gccactccct 1020
```

acactccccg tccgcaggat ccactcacca tcggagagga aacacgagcg ccagcccagg 1080
ccccctcggc cgcccctcgg ggaccggcca tccacaccag gcaccaaacc caacatctgt 1140
gacggcaact tcaacacagt ggccctcttc cggggcgaga tgtttgtctt taaggatcgc 1200
tggttctggc gtctgcgcaa taaccgagtg caggagggct accccatgca gatcgagcag 1260
ttctggaagg gcctgcctgc ccgcatcgac gcagcctatg aaagggccga tgggagattt 1320
gtcttcttca aaggtgacaa gtattgggtg tttaaggagg tgacggtgga gcctgggtac 1380
ccccacagcc tgggggagct gggcagctgt ttgccccgtg aaggcattga cacagctctg 1440
cgctgggaac ctgtgggcaa gacctacttt ttcaaaggcg agcggtactg gcgctacagc 1500
gaggagcggc gggccacgga ccctggctac cctaagccca tcaccgtgtg gaagggcatc 1560
ccaaggctc cccaaggagc cttcatcagc aaggaaggat attacaccta tttctacaag 1620
ggccgggact actggaagtt tgacaaccag aaactgagcg tggagccagg ctaccccgcg 1680
aacatcctgc gtgactggat gggctgcaac cagaaggagg tggagcggcg gaaggagcgg 1740
cggctgcccc aggacgacgt ggacatcatg gtgaccatca acgatgtgcc gggctccgtg 1800
aacgccgtgg ccgtggtcat cccctgcatc ctgtccctct gcatcctggt gctggtctac 1860
accatcttcc agttcaagaa caagacaggc cctcagcctg tcacctacta taagcggcca 1920
gtccaggaat gggtgtga 1938

<210> 77
<211> 1689
<212> DNA
<213> Homo sapiens

<300>
<302> MT6MMP
<310> AJ27137

<400> 77
atgcggctgc ggctccggct tctggcgctg ctgctttctgc tgctggcacc gcccgcgcgc 60
gccccgaagc cctcggcgca ggacgtgagc ctgggcgtgg actggctgac tcgctatggt 120
tacctgccgc caccccaccc tgcccaggcc cagctgcaga gccctgagaa gttgcgcgat 180
gccatcaaag tcatgcagag gttcgcgggg ctgccggaga ccggccgcat ggacccaggg 240
acagtggcca ccatgcgtaa gccccgctgc tccctgcctg acgtgctggg ggtggcgggg 300
ctggtcaggc ggcgtcgccg gtacgctctg agcggcagcg tgtggaagaa gcgaaccctg 360
acatggaggg tacgttcctt cccccagagc tcccagctga gccaggagac cgtgcgggtc 420
ctcatgagct atgccctgat ggcctggggc atggagtcag gcctcacatt tcatgaggtg 480
gattcccccc agggccagga gcccgacatc ctcatcgact ttgcccgcgc cttccaccag 540
gacagctacc ccttcgacgg gttggggggc accctagccc atgccttctt ccctgaggag 600
caccccatct ccggggacac tcactttgac gatgaggaga cctggacttt tgggtcaaaa 660
gacggcgagg ggaccgacct gtttgccgtg gctgtccatg agtttgccca cgccctgggc 720
ctgggccact cctcagcccc caactccatt atgaggccct tctaccaggg tccggtgggc 780
gacctgaca agtaccgcct gtctcaggat gaccgcgatg gcctgcagca actctatggg 840
aaggcgcccc aaaccccata tgacaagccc acaaggaaac ccctggctcc tccgccccag 900
ccccggcct cgcccacaca cagcccatcc ttccccatcc ctgatcgatg tgagggcaat 960
tttgacgcca tcgccaacat ccgaggggaa actttcttct tcaaaggccc ctggttctgg 1020
cgcctccagc cctccggaca gctggtgtcc ccgcgacccg cacggctgca ccgcttctgg 1080
gaggggctgc ccgcccaggt gagggtggtg caggccgcct atgctcggca ccgagacggc 1140
cgaatcctcc tctttagcgg gccccagttc tgggtgttcc aggaccggca gctggagggc 1200
ggggcgcggc cgctcacgga gctggggctg cccccgggag aggaggtgga cgccgtgttc 1260
tcgtggccac agaacgggaa gacctacctg gtccgcggcc ggcagtactg gcgctacgac 1320
gaggcggcgg cgcgcccgga ccccggctac cctcgcgacc tgagcctctg ggaaggcgcg 1380
ccccctcctc ctgacgatgt caccgtcagc aacgcaggtg acacctactt cttcaagggc 1440
gcccactact ggcgcttccc caagaacagc atcaagaccg agccggacgc cccccagccc 1500
atgggggcca actggctgga ctgccccgcc ccgagctctg gtccccgcgc ccccaggccc 1560
cccaaagcga ccccctgtc cgaaacctgc gattgtcagt gcgagctcaa ccaggccgca 1620
ggacgttggc ctgctcccat cccgctgctc ctcttgcccc tgctggtggg gggtgtagcc 1680
tcccgctga 1689

<210> 78

<211> 1749
<212> DNA
<213> Homo sapiens

<300>
<302> MTMMP
<310> X90925

<400> 78
atgtctcccg ccccaagacc ctcccgttgt ctcctgctcc ccctgctcac gctcggcacc 60
gcgctcgcct ccctcggctc ggcccaaagc agcagcttca gccccgaagc ctggctacag 120
caatatggct acctgcctcc cggggaccta cgtacccaca cacagcgctc accccagtca 180
ctctcagcgg ccatcgctgc catgcagaag ttttacggct tgcaagtaac aggcaaagct 240
gatgcagaca ccatgaaggc catgaggcgc ccccgatgtg gtgtttccaga caagtttggg 300
gctgagatca aggccaatgt tcgaaggaag cgctacgcca tccagggtct caaatggcaa 360
cataatgaaa tcactttctg catccagaat tacacccca aggtgggcga gtatgccaca 420
tacgaggcca ttcgcaaggc gttccgcgtg tgggagagtg ccacaccact gcgcttccgc 480
gaggtgccct atgcctacat ccgtgagggc catgagaagc aggccgacat catgatcttc 540
tttgccgagg gcttccatgg cgacagcacg cccttcgatg gtgagggcgg cttcctggcc 600
catgcctact tccaggccc caacattgga ggagacaccc actttgactc tgccgagcct 660
tggactgtca ggaatgagga tctgaatgga aatgacatct tcctggtggc tgtgcacgag 720
ctgggccatg ccctggggct cgagcattcc agtgacccct cggccatcat ggcacccttt 780
taccagtgga tggacacgga gaattttgtg ctgcccgatg atgaccgccg gggcatccag 840
caactttatg ggggtgagtc agggttcccc accaagatgc cccctcaacc caggactacc 900
tcccggcctt ctgttcctga taaacccaaa aaccccacct atgggcccaa catctgtgac 960
gggaactttg acaccgtggc catgctccga ggggagatgt ttgtcttcaa ggagcgctgg 1020
ttctggcggg tgaggaataa ccaagtgatg gatggatacc caatgcccat tggccagttc 1080
tggcggggcc tgcctgcgtc catcaacact gcctacgaga ggaaggatgg caaattcgtc 1140
ttcttcaaag gagacaagca ttgggtgttt gatgaggcgt ccctggaacc tggctacccc 1200
aagcacatta aggagctggg ccgagggctg cctaccgaca agattgatgc tgctctcttc 1260
tggatgccca atggaaagac ctacttcttc cgtggaaaca agtactaccg tttcaacgaa 1320
gagctcaggg cagtggatag cgagtacccc aagaacatca aagtctggga agggatccct 1380
gagtctccca gagggtcatt catgggcagc gatgaagtct tcacttactt ctacaagggg 1440
aacaaatact ggaaattcaa caaccagaag ctgaaggtag aaccgggcta ccccaagcca 1500
gccctgaggg actggatggg ctgcccatcg ggaggccggc cggatgaggg gactgaggag 1560
gagacggagg tgatcatcat tgaggtggac gaggagggcg gcgggggcgt gagcgcggct 1620
gccgtggtgc tgcccgtgct gctgctgctc ctggtgctgg cggtgggcct tgcagtcttc 1680
ttcttcagac gccatgggac ccccaggcga ctgctctact gccagcgttc cctgctggac 1740
aaggtctga 1749

<210> 79
<211> 744
<212> DNA
<213> Homo sapiens

<300>
<302> FGF1
<310> XM003647

<400> 79
atggccgcgg ccatcgctag cggcttgatc cgccagaagc ggcaggcgcg ggagcagcac 60
tgggaccggc cgtctgccag caggaggcgg agcagcccca gcaagaaccg cgggctctgc 120
aacggcaacc tggtggatat cttctccaaa gtgcgcatct tcggcctcaa gaagcgcagg 180
ttgcggcgcc aagatcccca gctcaagggt atagtgacca ggttatattg caggcaaggc 240
tactacttgc aaatgcaccc cgatggagct ctcgatggaa ccaaggatga cagcactaat 300
tctacactct tcaacctcat accagtggga ctacgtgttg ttgccatcca gggagtgaaa 360
acagggttgt atatagccat gaatggagaa ggttacctct acccatcaga acttttacc 420
cctgaatgca agtttaaaga atctgttttt gaaaattatt atgtaatcta ctcatccatg 480
ttgtacagac aacaggaatc tggtagagcc tggttttgg gattaaataa ggaagggcaa 540

gctatgaaag ggaacagagt aaagaaaacc aaaccagcag ctcatttttct acccaagcca 600
ttggaagttg ccatgtaccg agaaccatct ttgcatgatg ttgggggaaac ggtcccgaag 660
cctgggggtga cgccaagtaa aagcacaagt gcgtctgcaa taatgaatgg aggcaaacca 720
gtcaacaaga gtaagacaac atag 744

<210> 80
<211> 468
<212> DNA
<213> Homo sapiens

<300>
<302> FGF2
<310> NM002006

<400> 80
atggcagccg ggagcatcac cacgctgccc gccttgcccg aggatggcgg cagcggcgcc 60
ttcccgcccg gccacttcaa ggaccccaag cggctgtact gcaaaaacgg gggcttcttc 120
ctgcgcatcc accccgacgg ccgagttgac ggggtccggg agaagagcga ccctcacatc 180
aagctacaac ttcaagcaga agagagagga gttgtgtcta tcaaaggagt gtgtgctaac 240
cgttacctgg ctatgaagga agatggaaga ttactggctt ctaaatgtgt tacggatgag 300
tgttttcttt ttgaacgatt ggaatctaat aactacaata cttaccggtc aaggaaatac 360
accagttggt atgtggcact gaaacgaact gggcagtata aacttggatc caaaacagga 420
cctgggcaga aagctatact ttttcttcca atgtctgcta agagctga 468

<210> 81
<211> 756
<212> DNA
<213> Homo sapiens

<300>
<302> FGF23
<310> NM020638

<400> 81
atgttggggg cccgcctcag gctctgggtc tgtgccttgt gcagcgtctg cagcatgagc 60
gtcctcagag cctatcccaa tgcctcccca ctgctcggct ccagctgggg tggcctgatc 120
cacctgtaca cagccacagc caggaacagc taccacctgc agatccacaa gaatggccat 180
gtggatggcg caccccatca gaccatctac agtgccctga tgatcagatc agaggatgct 240
ggctttgtgg tgattacagg tgtgatgagc agaagatacc tctgcatgga tttcagaggc 300
aacatttttg gatcacacta tttcgacccg gagaactgca ggttccaaca ccagacgctg 360
gaaaacgggt acgacgtcta ccactctcct cagtatcact tcctggtcag tctgggccgg 420
gcgaagagag ccttcctgcc aggcatgaac ccaccccgt actcccagtt cctgtcccgg 480
aggaacgaga tccccctaat tcacttcaac accccatac cacggcggca cacccggagc 540
gccgaggacg actcggagcg ggaccccctg aacgtgctga agccccgggc ccggatgacc 600
ccggccccgg cctcctgttc acaggagctc ccgagcgccg aggacaacag cccgatggcc 660
agtgacccat taggggtggt caggggcggt cgagtgaaca cgcacgctgg gggaacgggc 720
ccggaaggct gccgcccctt cgccaagttc atctag 756

<210> 82
<211> 720
<212> DNA
<213> Homo sapiens

<300>
<302> FGF3
<310> NM005247

<400> 82
atgggcctaa tctggctgct actgctcagc ctgctggagc ccggctggcc cgcagcgggc 60
cctggggcgc ggttgcggcg cgatgcgggc ggccgtggcg gcgtctacga gcaccttggc 120
ggggcgccct ggcgccgcaa gctctactgc gccacgaagt accacctcca gctgcacccg 180
agcggccgcg tcaacggcag cctggagaac agcgcctaca gtatttgga gataacggca 240
gtggaggtgg gcattgtggc catcaggggt ctcttctccg ggcggtacct ggccatgaac 300
aagaggggac gactctatgc ttcggagcac tacagcgccg agtgcgagtt tgtggagcgg 360
atccacgagc tgggctataa tacgtatgcc tcccggctgt accggacggt gtctagtacg 420
cctggggccc gccggcagcc cagcgccgag agactgtggt acgtgtctgt gaacggcaag 480
ggccggcccc gcaggggctt caagacccgc cgcacacaga agtcctccct gttctgccc 540
cgcgtgctgg accacaggga ccacgagatg gtgcggcagc tacagagtgg gctgcccaga 600
ccccctggta agggggtcca gccccgacgg cggcggcaga agcagagccc ggataacctg 660
gagccctctc acgttcaggc ttcgagactg ggctcccagc tggaggccag tgcgcactag 720

<210> 83
<211> 807
<212> DNA
<213> Homo sapiens

<300>
<302> FGF5
<310> NM004464

<400> 83
atgagcttgt ccttcctcct cctcctcttc ttcagccacc tgatcctcag cgcctgggct 60
cacgggggaga agcgtctcgc ccccaaaggg caaccggac ccgctgccac tgataggaac 120
cctataggct ccagcagcag acagagcagc agtagcgcta tgtcttcctc ttctgcctcc 180
tcctccccg cagcttctct gggcagccaa ggaagtggct tggagcagag cagtttccag 240
tggagcccct cggggcgccg gaccggcagc ctctactgca gagtgggcat cggttccat 300
ctgcagatct acccggatgg caaagtcaat ggatcccacg aagccaatat gttaagtgtt 360
ttggaaatat ttgctgtgtc tcaggggatt gtaggaatac gaggagtttt cagcaacaaa 420
tttttagcga tgtcaaaaaa aggaaaactc catgcaagtg ccaagttcac agatgactgc 480
aagttcaggg agcgttttca agaaaatagc tataatacct atgcctcagc aatacataga 540
actgaaaaaa cagggcggga gtggtatgtt gccctgaata aaagaggaaa agccaaacga 600
gggtgcagcc cccgggttaa accccagcat atctctaccc attttcttcc aagattcaag 660
cagtcggagc agccagaact ttctttcacg gttactgttc ctgaaaagaa aaatccacct 720
agccctatca agtcaaagat tcccctttct gcacctcgga aaaataccaa ctcagtgaaa 780
tacagactca agtttcgctt tggataa 807

<210> 84
<211> 649
<212> DNA
<213> Homo sapiens

<300>
<302> FGF8
<310> NM006119

<400> 84
atgggcagcc cccgctccgc gctgagctgc ctgctgttgc acttgctggt cctctgcctc 60
caagcccagg taactgttca gtcctcacct aattttacac agcatgtgag ggagcagagc 120
ctggtgacgg atcagctcag ccgccgcctc atccggacct accaactcta cagccgcacc 180
agcgggaagc acgtgcaggt cctggccaac aagcgcatca acgccatggc agaggacggc 240
gaccccttcg caaagctcat cgtggagacg gacaccttg gaagcagagt tcgagtccga 300
ggagccgaga cgggcctcta catctgcatg aacaagaagg ggaagctgat cgccaagagc 360
aacggcaaag gcaaggactg cgtcttcacg gagattgtgc tggagaacaa ctacacagcg 420
ctgcagaatg ccaagtacga gggctggtac atggccttca cccgcaaggg ccgccccgc 480
aagggctcca agacgcggca gcaccagcgt gaggtccact tcatgaagcg gctgccccgg 540

ggccaccaca ccaccgagca gagcctgcgc ttcgagttcc tcaactaccc gcccttcacg 600
cgcagcctgc gcggcagcca gaggacttgg gccccggaac cccgatagg 649

<210> 85
<211> 2466
<212> DNA
<213> Homo sapiens

<300>
<302> FGFR2
<310> NM000141

<400> 85
atggtcagct ggggtcgttt catctgcctg gtcgtggtca ccatggcaac cttgtccctg 60
gcccggccct ccttcagttt agttgaggat accacattag agccagaaga gccaccaacc 120
aaatacctaa tctctcaacc agaagtgtac gtggctgcgc cagggagtc gctagaggtg 180
cgctgcctgt tgaaagatgc cgccgtgatc agttggacta aggatggggt gcacttgggg 240
cccaacaata ggacagtgct tattggggag tacttgcaga taaagggcgc cacgcctaga 300
gactccggcc tctatgcttg tactgccagt aggactgtag cagttgaaac ttggtacttc 360
atggtgaatg tcacagatgc catctcatcc ggagatgatg aggatgacac cgatggtgcg 420
gaagattttg tcagtgagaa cagtaacaac aagagagcac catactggac caacacagaa 480
aagatggaaa agcggctcca tgctgtgcct gcggccaaca ctgtcaagtt tcgctgccca 540
gccgggggga acccaatgcc aaccatgcgg tggctgaaaa acgggaagga gtttaagcag 600
gagcatcgca ttggaggcta caaggtacga aaccagcact ggagcctcat tatggaaagt 660
gtggtcccat ctgacaaggg aaattatacc tgtgtggtgg agaatgaata cgggtccatc 720
aatcacacgt accacctgga tgttgtggag cgatcgcctc accggcccat cctccaagcc 780
ggactgccgg caaatgcctc cacagtggtc ggaggagacg tagagtttgt ctgcaaggtt 840
tacagtgatg cccagcccca catccagtgg atcaagcacg tggaaaagaa cggcagtaaa 900
tacgggccca acgggctgcc ctacctcaag gttctcaagg ccgccggtgt taacaccacg 960
gacaaagaga ttgaggttct ctatattcgg aatgtaactt ttgaggacgc tggggaatat 1020
acgtgcttgg cgggtaattc tattgggata tcctttcact ctgcatggtt gacagttctg 1080
ccagcgcctg gaagagaaaa ggagattaca gcttccccag actacctgga gatagccatt 1140
tactgcatag gggtcttctt aatcgcctgt atggtggtaa cagtcatcct gtgccgaatg 1200
aagaacacga ccaagaagcc agacttcagc agccagccgg ctgtgcacaa gctgaccaaa 1260
cgtatccccc tgcggagaca ggtaacagtt tcggctgagt ccagctcctc catgaactcc 1320
aacccccgc tggtgaggat aacaacacgc ctctcttcaa cggcagacac ccccatgctg 1380
gcaggggtct ccgagtatga acttccagag gacccaaaat gggagtttcc aagagataag 1440
ctgacactgg gcaagccccct gggagaaggt tgctttgggc aagtggtcat ggcggaagca 1500
gtgggaattg acaaagacaa gcccaaggag gcggtcaccg tggccgtgaa gatgttgaaa 1560
gatgatgcca cagagaaaga cctttctgat ctggtgtcag agatggagat gatgaagatg 1620
attgggaaac acaagaatat cataaatctt cttggagcct gcacacagga tgggcctctc 1680
tatgtcatag ttgagtatgc ctctaaaggc aacctccgag aatacctccg agcccggagg 1740
ccacccggga tggagtactc ctatgacatt aaccgtgttc ctgaggagca gatgaccttc 1800
aaggacttgg tgtcatgcac ctaccagctg gccagaggca tggagtactt ggcttcccaa 1860
aaatgtattc atcgagattt agcagccaga aatgttttgg taacagaaaa caatgtgatg 1920
aaaatagcag actttggact cgccagagat atcaacaata tagactatta caaaaagacc 1980
accaatgggc ggcttccagt caagtggatg gctccagaag ccctgtttga tagagtatac 2040
actcatcaga gtgatgtctg gtccttcggg gtgttaatgt gggagatctt cactttaggg 2100
ggctcgccct acccagggat tcccgtggag gaacttttta agctgctgaa gaaggacac 2160
agaatggata agccagccaa ctgcaccaac gaactgtaca tgatgatgag ggactgttgg 2220
catgcagtgc cctcccagag accaacgttc aagcagttgg tagaagactt ggatcgaatt 2280
ctcactctca caaccaatga ggaatacttg gacctcagcc aacctctcga acagtattca 2340
cctagttacc ctgacacaag aagttcttgt tcttcaggag atgattctgt tttttctcca 2400
gaccccatgc cttacgaacc atgccttcct cagtatccac acataaacgg cagtgttaaa 2460
acatga 2466

<210> 86
<211> 2421

<212> DNA
<213> Homo sapiens

<300>
<302> FGFR3
<310> NM000142

<400> 86
atgggcgccc ctgcctgcgc cctcgcgctc tgcgtggccg tggccatcgt ggccggcgcc 60
tcctcggagt ccttggggac ggagcagcgc gtcgtgggcg gagcggcaga agtcccgggc 120
ccagagcccg gccagcagga gcagttggtc ttcggcagcg gggatgctgt ggagctgagc 180
tgtccccgcc ccgggggtgg tcccatgggg cccactgtct gggtcaagga tggcacaggg 240
ctggtgccct cggagcgtgt cctggtgggg ccccagcggc tgcaggtgct gaatgcctcc 300
cacgaggact ccgggggcct agctgccgg cagcggctca cgcagcgcgt actgtgccac 360
ttcagtgtgc gggtgacaga cgctccatcc tcgggagatg acgaagacgg ggaggacgag 420
gctgaggaca caggtgtgga cacaggggcc ccttactgga cacggcccga gcggatggac 480
aagaagctgc tggccgtgcc ggccgccaac accgtccgct tccgctgccc agccgctggc 540
aaccccactc cctccatctc ctggctgaag aacggcaggg agttccgcgg cgagcaccgc 600
attggaggca tcaagctgcg gcatcagcag tggagcctgg tcatggaaag cgtggtgccc 660
tcggaccgcg gcaactacac ctgcgtcgtg gagaacaagt ttggcagcat ccggcagacg 720
tacacgctgg acgtgctgga gcgctccccg caccggccca tcctgcaggc ggggctgccg 780
gccaaccaga cggcggtgct gggcagcgac gtggagttcc actgcaaggt gtacagtgac 840
gcacagcccc acatccagtg gctcaagcac gtggaggtga acggcagcaa ggtggtgccc 900
gacggcacac cctacgttac cgtgctcaag acggcgggcg ctaacaccac cgacaaggag 960
ctagaggttc tctccttgca caacgtcacc tttgaggacg ccggggagta cacctgcctg 1020
gcgggcaatt ctattgggtt ttctcatcac tctgcgtggc tggtggtgct gccagccgag 1080
gaggagctgg tggaggctga cgaggcgggc agtgtgtatg caggcatcct cagctacggg 1140
gtgggcttct tcctgttcat cctggtggtg gcggctgtga cgctctgccg cctgcgcagc 1200
ccccccaaga aaggcctggg ctcccccacc gtgcacaaga tctcccgctt cccgctcaag 1260
cgacaggtgt ccctggagtc caacgcgtcc atgagctcca acacaccact ggtgcgcatc 1320
gcaaggctgt cctcagggga gggccccacg ctggccaatg tctccgagct cgagctgcct 1380
gccgacccca aatgggagct gtctcgggcc cggctgaccc tgggcaagcc ccttggggag 1440
ggctgcttcg gccaggtggt catggcggag gccatcggca ttgacaagga ccggggccgc 1500
aagcctgtca ccgtagccgt gaagatgctg aaagacgatg ccactgacaa ggacctgtcg 1560
gacctggtgt ctgagatgga gatgatgaag atgatcggga aacacaaaaa catcatcaac 1620
ctgctgggcg cctgcacgca gggcgggccc ctgtacgtgc tggtggagta cgcggccaag 1680
ggtaacctgc gggagtttct gcgggcgcgg cggccccccg gcctggacta ctccttcgac 1740
acctgcaagc cgcccgagga gcagctcacc ttcaaggacc tggtgtcctg tgcctaccag 1800
gtggcccggg gcatggagta cttggctcac cagaagtgca tccacaggga cctggctgcc 1860
cgcaatgtgc tggtgaccga ggacaacgtg atgaagatcg cagacttcgg gctggcccgg 1920
gacgtgcaca acctcgacta ctacaagaag acaaccaacg gccggctgcc cgtgaagtgg 1980
atggcgcctg aggccttgtt tgaccgagtc tacactcacc agagtgacgt ctggtccttt 2040
ggggtcctgc tctgggagat cttcacgctg gggggctccc cgtaccccgg catccctgtg 2100
gaggagctct tcaagctgct gaaggagggc caccgcatgg acaagcccgc caactgcaca 2160
cacgacctgt acatgatcat gcgggagtgc tggcatgccg cgccctccca gaggcccacc 2220
ttcaagcagc tggtggagga cctggaccgt gtccttaccg tgacgtccac cgacgagtac 2280
ctggacctgt cggcgccttt cgagcagtac tccccgggtg ggccaggacac ccccagctcc 2340
agctcctcag gggacgactc cgtgtttgcc cacgacctgc tgccccggcc cccacccagc 2400
agtgggggct cgcggacgtg a 2421

<210> 87
<211> 2102
<212> DNA
<213> Homo sapiens

<300>
<302> HGF
<310> E08541

<400> 87
atgcagaggg acaaaggaaa agaagaaata caattcatga attcaaaaaa tcagcaaaga 60
ctaccctaat caaaatagat ccagcactga agataaaaac caaaaaagtg aatactgcag 120
accaatgtgc taatagatgt actaggaata aaggacttcc attcacttgc aaggctttg 180
tttttgataa agcaagaaaa caatgcctct ggttcccctt caatagcatg tcaagtggag 240
tgaaaaaaga atttggccat gaatttgacc tctatgaaaa caaagactac attagaaact 300
gcatcattgg taaaggacgc agctacaagg gaacagtatc tatcactaag agtggcatca 360
aatgtcagcc ctggagttcc atgataccac acgaacacag ctttttgcct tcgagctatc 420
ggggtaaaga cctacaggaa aactactgtc gaaatcctcg aggggaagaa gggggaccct 480
ggtgtttcac aagcaatcca gaggtacgct acgaagtctg tgacattcct cagtgttcag 540
aagttgaatg catgacctgc aatggggaga gttatcgagg tctcatggat catacagaat 600
caggcaagat ttgtcagcgc tgggatcatc agacaccaca ccggcacaaa ttcttgcctg 660
aaagatatcc cgacaagggc tttgatgata attattgccg caatcccgat ggccagccga 720
ggccatggtg ctatactctt gaccctcaca cccgctggga gtactgtgca attaaaacat 780
gcgctgacaa tactatgaat gacactgatg ttccttgga aacaactgaa tgcatccaag 840
gtcaaggaga aggctacagg ggcactgtca ataccatttg gaatggaatt ccatgtcagc 900
gttgggattc tcagtatcct cacgagcatg acatgactcc tgaaaatttc aagtgcaagg 960
acctacgaga aaattactgc cgaaatccag atgggtctga atcaccctgg tgttttacca 1020
ctgatccaaa catccgagtt ggctactgct cccaaatttcc aaactgtgat atgtcacatg 1080
gacaagattg ttatcgtggg aatggcaaaa attatatggg caacttatcc caaacaagat 1140
ctggactaac atgttcaatg tgggacaaga acatggaaga cttacatcgt catatcttct 1200
gggaaccaga tgcaagtaag ctgaatgaga attactgccg gatgatgctc 1260
atggaccctg gtgctacacg ggaaatccac tcattccttg ggattattgc cctatttctc 1320
gttgtgaagg tgataccaca cctacaatag tcaatttaga ccatcccgta atatcttgtg 1380
ccaaaaggaa acaattgcga gttgtaaatg ggattccaac acgaacaaac ataggatgga 1440
tggttagttt gagatacaga aataaacata tctgcggagg atcattgata aaggagagtt 1500
gggttcttac tgcacgacag tgtttccctt ctcgagactt gaaagattat gaagcttggc 1560
ttggaattca tgatgtccac ggaagaggag atgagaaatg caaacaggtt ctcaatgttt 1620
cccagctggt atatggccct gaaggatcag atctggtttt aatgaagctt gccaggcctg 1680
ctgtcctgga tgattttgtt agtacgattg atttacctaa ttatggatgc acaattcctg 1740
aaaagaccag ttgcagtgtt tatggctggg gctacactgg attgatcaac tatgatggcc 1800
tattacgagt ggcacatctc tatataatgg gaaatgagaa atgcagccag catcatcgag 1860
ggaaggtgac tctgaatgag tctgaaatat gtgctggggc tgaaaagatt ggatcaggac 1920
catgtgaggg ggattatggt ggcccacttg tttgtgagca acataaaatg agaatggttc 1980
ttggtgtcat tgttcctggt cgtggatgtg ccattccaaa tcgtcctggt atttttgtcc 2040
gagtagcata ttatgcaaaa tggatacaca aaattatttt aacatataag gtaccacagt 2100
ca 2102

<210> 88
<211> 360
<212> DNA
<213> Homo sapiens

<300>
<302> ID3
<310> XM001539

<400> 88
atgaaggcgc tgagcccggt gcgcggctgc tacgaggcgg tgtgctgcct gtcggaacgc 60
agtctggcca tcgccgggag ccgagggaag ggccccggcag ctgaggagcc gctgagcttg 120
ctggacgaca tgaaccactg ctactcccgc ctgcgggaac tggtacccgg agtcccgaga 180
ggcactcagc ttagccaggt ggaaatccta cagcgcgtca tcgactacat tctcgacctg 240
caggtagtcc tggccgagcc agcccctgga ccccctgatg gccccacact tcccatccag 300
acagccgagc tcactccgga acttgtccatc tccaacgaca aaaggagctt ttgccactga 360

<210> 89
<211> 743
<212> DNA

<213> Homo sapiens

<300>
<302> IGF2
<310> NM000612

<400> 89
atgggaatcc caatggggaa gtcgatgctg gtgcttctca ccttcttggc cttcgcctcg 60
tgctgcattg ctgcttaccg ccccagtgag accctgtgcg gcggggagct ggtggacacc 120
ctccagttcg tctgtgggga ccgcggcttc tacttcagca ggccccgcaag ccgtgtgagc 180
cgtcgcagcc gtggcatcgt tgaggagtgc tgtttccgca gctgtgacct ggccctcctg 240
gagacgtact gtgctacccc cgccaagtcc gagagggacg tgtcgacccc tccgaccgtg 300
cttccggaca acttccccag ataccccgtg ggcaagttct tccaatatga cacctggaag 360
cagtccaccc agcgcctgcg caggggcctg cctgccctcc tgcgtgcccg ccggggtcac 420
gtgctcgcca aggagctcga ggcgttcagg gaggccaaac gtcaccgtcc cctgattgct 480
ctacccaccc aagaccccgc ccacgggggc gccccccag agatggccag caatcggaag 540
tgagcaaaac tgccgcaagt ctgcagcccg gcgccaccat cctgcagcct cctcctgacc 600
acggacgttt ccatcaggtt ccatcccgaa aatctctcgg ttccacgtcc cctggggct 660
tctcctgacc cagtccccgt gccccgcctc cccgaaacag gctactctcc tcggcccct 720
ccatcgggct gaggaagcac agc 743

<210> 90
<211> 7476
<212> DNA
<213> Homo sapiens

<300>
<302> IGF2R
<310> NM000876

<400> 90
atgggggccg ccgccggccg gagcccccac ctggggcccg cgcccgcccg ccgcccgcag 60
cgctctctgc tcctgctgca gctgctgctg ctcgtcgctg ccccggggtc cacgcaggcc 120
caggccgccc cgttccccga gctgtgcagt tatacatggg aagctgttga taccaaaaat 180
aatgtacttt ataaaatcaa catctgtgga agtgtggata ttgtccagtg cgggccatca 240
agtgctgttt gtatgcacga cttgaagaca cgcacttatc attcagtggg tgactctgtt 300
ttgagaagtg caaccagatc tctcctggaa ttcaacacaa cagtgagctg tgaccagcaa 360
ggcacaaatc acagagtcca gagcagcatt gccttcctgt gtgggaaaac cctgggaact 420
cctgaatttg taactgcaac agaatgtgtg cactactttg agtggaggac cactgcagcc 480
tgcaagaaag acatatttaa agcaaataag gaggtgccat gctatgtgtt tgatgaagag 540
ttgaggaagc atgatctcaa tcctctgatc aagcttagtg gtgcctactt ggtggatgac 600
tccgatccgg acacttctct attcatcaat gtttgtagag acatagacac actacgagac 660
ccaggttcac agctgcgggc ctgtcccccc ggcactgccg cctgcctggt aagaggacac 720
caggcgtttg atgttggcca gccccgggac ggactgaagc tggtgcgcaa ggacaggctt 780
gtcctgagtt acgtgaggga agaggcagga aagctagact tttgtgatgg tcacagccct 840
gcggtgacta ttacatttgt ttgcccgtcg gagcggagag agggcaccat tcccaaactc 900
acagctaaat ccaactgccg ctatgaaatt gagtggatta ctgagtatgc ctgccacaga 960
gattacctgg aaagtaaaac ttgttctctg agcggcgagc agcaggatgt ctccatagac 1020
ctcacaccac ttgcccagag cggaggttca tcctatattt cagatggaaa agaatatttg 1080
tttatttga atgtctgtgg agaaactgaa atacagttct gtaataaaaa acaagctgca 1140
gtttgccaag tgaaaaagag cgatacctct caagtcaaag cagcaggaag atacacaat 1200
cagacctcc gatattcgga tggagacctc accttgatat atttggagg tgatgaatgc 1260
agctcagggt ttcagcggat gagcgtcata aactttgagt gcaataaaac cgcaggtaac 1320
gatgggaaag gaactcctgt attcacaggg gaggttgact gcacctactt cttcacatgg 1380
gacaggaat acgcctgtgt taaggagaag gaagacctcc tctgcggtgc caccgacggg 1440
aagaagcgct atgacctgtc cgcgctggtc cgccatgcag aaccagagca gaattgggaa 1500
gctgtggatg gcagtcagac ggaaacagag aagaagcatt ttttcattaa tatttgtcac 1560
agagtgctgc aggaaggcaa ggcacgaggg tgtcccgagg acgcggcagt gtgtgcagtg 1620
gataaaaatg gaagtaaaaa tctgggaaaa tttatttcct ctcccatgaa agagaaagga 1680

aacattcaac tctcttattc agatggtgat gattgtggtc atggcaagaa aattaaaact 1740
aatatcacac ttgtatgcaa gccaggtgat ctggaaagtg caccagtgtt gagaacttct 1800
ggggaaggcg gttgctttta tgagtttgag tggcgcacag ctgcggcctg tgtgctgtct 1860
aagacagaag gggagaactg cacggtcttt gactcccagg cagggttttc ttttgactta 1920
tcacctctca caaagaaaaa tggtgcctat aaagttgaga caaagaagta tgacttttat 1980
ataaatgtgt gtggcccggt gtctgtgagc ccctgtcagc cagactcagg agcctgccag 2040
gtggcaaaaa gtgatgagaa gacttggaac ttgggtctga gtaatgcgaa gctttcatat 2100
tatgatggga tgatccaact gaactacaga ggcggcacac cctataacaa tgaaagacac 2160
acaccgagag ctacgctcat caccttctc tgtgatcgag acgcgggagt gggcttccct 2220
gaatatcagg aagaggataa ctccacctac aacttccggt ggtacaccag ctatgcctgc 2280
ccggaggagc ccctggaatg cgtagtgacc gacccctcca cgctggagca gtacgacctc 2340
tccagtctgg caaaatctga aggtggcctt ggaggaaact ggtatgccat ggacaactca 2400
ggggaacatg tcacgtggag gaaatactac attaacgtgt gtcggcctct gaatccagtg 2460
ccgggctgca accgatatgc atcggcttgc cagatgaagt atgaaaaaga tcaggggctcc 2520
ttcactgaag tggtttccat cagtaacttg ggaatggcaa agaccggccc ggtggttgag 2580
gacagcggca gcctccttct ggaatacgtg aatgggtcgg cctgcaccac cagcgatggc 2640
agacagacca catataccac gaggatccat ctcgtctgct ccaggggcag gctgaacagc 2700
caccccatct tttctctcaa ctgggagtgt gtggtcagtt tcctgtggaa cacagaggct 2760
gcctgtccca ttcagacaac gacggataca gaccaggctt gctctataag ggatcccaac 2820
agtggatttg tgtttaatct taatccgcta aacagttcgc aaggatataa cgtctctggc 2880
attgggaaga tttttatgtt taatgtctgc ggcacaatgc ctgtctgtgg gaccatcctg 2940
ggaaaacctg cttctggctg tgaggcagaa acccaaactg aagagctcaa gaattggaag 3000
ccagcaaggc cagtcggaat tgagaaaagc ctccagctgt ccacagaggg cttcatcact 3060
ctgacctaca aagggcctct ctctgccaaa ggtaccgctt atgcttttat cgtccgcttt 3120
gtttgcaatg atgatgttta ctcagggccc ctcaaatttcc tgcatcaaga tatcgactct 3180
gggcaaggga tccgaaacac ttactttgag tttgaaaccg cgttggcctg tgttccttct 3240
ccagtggact gccaagtcac cgacctggct ggaaatgagt acgacctgac tggcctaagc 3300
acagtcagga aaccttggac ggctgttgac acctctgtcg atgggagaaa gagcagtttc 3360
tatttgagcg tttgcaatcc tctccttac attcctggat gccagggcag cgcagtgggg 3420
tcttgcttag tgtcagaagg caatagctgg aatctgggtg tggtgcagat gagtccccaa 3480
gccgcggcga atggatcttt gagcatcatg tatgtcaacg gtgacaagtg tgggaaccag 3540
cgcttctcca ccaggatcac gtttgagtgt gctcagatat cgggctcacc agcatttcag 3600
cttcaggatg gttgtgagta cgtgtttatc tggagaactg tggaagcctg tccgttgtc 3660
agagtggaag gggacaactg tgaggtgaaa gacccaaggc atggcaactt gtatgacctg 3720
aagccccttg gcctcaacga caccatcgtg agcgctggcg aatacactta ttacttccgg 3780
gtctgtggga agctttcctc agacgtctgc cccacaagtg acaagtccaa ggtggtctcc 3840
tcatgtcagg aaaagcggga accgcaggga tttcacaaag tggcaggtct cctgactcag 3900
aagctaactt atgaaaatgg cttgttaaaa atgaacttca cggggggga cacttgccat 3960
aaggtttatc agcgctccac agccatcttc ttctactgtg accgcggcac ccagcggcca 4020
gtatttctaa aggagacttc agattgttcc tacttgtttg agtggcgaac gcagtatgcc 4080
tgcccacctt tcgatctgac tgaatgttca ttcaaagatg gggctggcaa ctccttcgac 4140
ctctcgtccc tgtcaaggta cagtgacaac tgggaagcca tcactgggac gggggacccg 4200
gagcactacc tcatcaatgt ctgcaagtct ctggcccgc aggctggcac tgagccgtgc 4260
cctccagaag cagccgcgtg tctgctgggt ggctccaagc ccgtgaacct cggcagggta 4320
agggacggac ctcagtggag agatggcata attgtcctga aatacgttga tggcgactta 4380
tgtccagatg ggattcggaa aaagtcaacc accatccgat tcacctgcag cgagagccaa 4440
gtgaactcca ggcccatgtt catcagcgcc gtggaggact gtgagtacac ctttgcctgg 4500
cccacagcca cagcctgtcc catgaagagc aacgagcatg atgactgcca ggtcaccaac 4560
ccaagcacag gacacctgtt tgatctgagc tccttaagtg gcagggcggg attcacagct 4620
gcttacagcg agaaggggtt ggtttacatg agcatctgtg gggagaatga aaactgccct 4680
cctggcgtgg gggcctgctt tggacagacc aggattagcg tgggcaaggc caacaagagg 4740
ctgagatacg tggaccaggt cctgcagctg gtgtacaagg atgggtcccc ttgtccctcc 4800
aaatccggcc tgagctataa gagtgtgatc agtttcgtgt gcagggcctga ggcgggcca 4860
accaatagge ccatgctcat ctccctggac aagcagacat gcactctctt ctttcctgg 4920
cacacgcgc tggcctgcga gcaagcgacc gaatgttccg tgaggaatgg aagctctatt 4980
gttgacttgt ctcccctttat tcatcgcact ggtggttatg aggcttatga tgagagtgag 5040
gatgatgcct ccgataccaa ccctgatttc tacatcaata tttgtcagcc actaaatccc 5100
atgcacgcag tgccctgtcc tgccggagcc gctgtgtgca aagttcctat tgatggtccc 5160
cccatagata tcggccgggt agcaggacca ccaatactca atccaatagc aaatgagatt 5220
tacttgaatt tgaaagcag tactccttgc ttagcggaca agcatttcaa ctacacctcg 5280

ctcatcgcgt ttcactgtaa gagaggtgtg agcatgggaa cgcctaagct gttaaggacc 5340
agcgagtgcg actttgtgtt cgaatgggag actcctgtcg tctgtcctga tgaagtgagg 5400
atggatggct gtaccctgac agatgagcag ctcctctaca gcttcaactt gtccagcctt 5460
tccacgagca cctttaaggt gactcgcgac tcgcgcacct acagcgttgg ggtgtgcacc 5520
tttgcagtcg ggccagaaca aggaggctgt aaggacggag gagtctgtct gctctcaggc 5580
accaaggggg catccttttgg acggctgcaa tcaatgaaac tggattacag gcaccaggat 5640
gaagcggtcg ttttaagtta cgtgaatggt gatcgttgcc ctccagaaac cgatgacggc 5700
gtccccgtgg tcttcccctt catattcaat gggaagagct acgaggagtg catcatagag 5760
agcagggcga agctgtggtg tagcacaact gcggactacg acagagacca cgagtggggc 5820
ttctgcagac actcaaacag ctaccggaca tccagcatca tatttaagtg tgatgaagat 5880
gaggacattg ggaggccaca agtctttcagt gaagtgcgtg ggtgtgatgt gacatttgag 5940
tggaaaacaa aagttgtctg cccttccaaag aagttggagt gcaaatttgt ccagaaacac 6000
aaaacctacg acctgcggct gctctcctct ctcaccgggt cctggtccct ggtccacaac 6060
ggagtctcgt actatataaa tctgtgccag aaaatatata aagggcccct gggctgctct 6120
gaaagggcca gcatttgcag aaggaccaca actggtgacg tccaggtcct gggactcgtt 6180
cacacgcaga agctgggtgt cataggtgac aaagttgttg tcacgtactc caaaggttat 6240
ccgtgtggtg gaaataagac cgcatcctcc gtgatagaat tgacctgtac aaagacggtg 6300
ggcagacctg cattcaagag gtttgatatc gacagctgca cttactactt cagctgggac 6360
tcccgggctg cctgcgccgt gaagcctcag gaggtgcaga tggtgaatgg gaccatcacc 6420
aaccctataa atggcaagag cttcagcctc ggagatattt attttaagct gttcagagcc 6480
tctggggaca tgaggaccaa tggggacaac tacctgtatg agatccaact ttcctccatc 6540
acaagctcca gaaacccggc gtgctctgga gccaacatat gccaggtgaa gcccaacgat 6600
cagcacttca gtcggaaagt tggaacctct gacaagacca agtactacct tcaagacggc 6660
gatctcgatg tcgtgtttgc ctcttcctct aagtgcggaa aggataagac caagtctgtt 6720
tcttccacca tcttcttcca ctgtgaccct ctggtggagg acgggatccc cgagttcagt 6780
cacgagactg ccgactgcca gtacctcttc tcttggtaca cctcagccgt gtgtcctctg 6840
ggggtgggct ttgacagcga gaatcccggg gacgacgggc agatgcacaa gggggctgtca 6900
gaacggagcc aggcagtcgg cgcggtgctc agcctgctgc tggtggcgct cactcgtgc 6960
ctgctggccc tgttgctcta caagaaggag aggagggaaa cagtgataag taagctgacc 7020
acttgctgta ggagaagttc caacgtgtcc tacaaatact caaaggtgaa taaggaagaa 7080
gagacagatg agaatgaaac agagtggctg atggaagaga tccagctgcc tcctccacgg 7140
cagggaaagg aagggcagga gaacggccat attaccacca agtcagtgaa agccctcagc 7200
tccctgcatg gggatgacca ggacagtgag gatgaggttc tgaccatccc agaggtgaaa 7260
gttcactcgg gcaggggagc tggggcagag agctccacac cagtgagaaa cgcacagagc 7320
aatgcccttc aggagcgtga ggacgatagg gtggggctgg tcaggggtga gaaggcgagg 7380
aaaggggaagt ccagctctgc acagcagaag acagtgagct ccaccaagct ggtgtccttc 7440
catgacgaca gcgacgagga cctcttacac atctga 7476

<210> 91
<211> 4104
<212> DNA
<213> Homo sapiens

<300>
<302> IGF1R
<310> NM000875

<400> 91
atgaagtctg gctccggagg agggtccccg acctcgctgt gggggctcct gtttctctcc 60
gccgcgctct cgctctggcc gacgagtgga gaaatctgcg ggccaggcat cgacatccgc 120
aacgactatc agcagctgaa gcgcctggag aactgcacgg tgatcgaggg ctacctccac 180
atcctgctca tctccaaggc cgaggactac cgcagctacc gcttccccaa gctcacggtc 240
attaccgagt acttgctgct gttccgagtg gctggcctcg agagcctcgg agacctcttc 300
ccgaacctca cggtcatccg cggctggaaa ctctttctaca actacgccct ggtcatcttc 360
gagatgacca atctcaagga tattgggctt tacaacctga ggaacattac tcgggggggc 420
atcaggattg agaaaaatgc tgaccttctgt tacctctcca ctgtggactg gtccctgatc 480
ctggatgcgg tgtccaataa ctacattgtg gggaataagc ccccaaagga atgtggggac 540
ctgtgtccag ggaccatgga ggagaagccg atgtgtgaga agacccaccat caacaatgag 600
tacaactacc gctgctggac cacaaaccgc tgccagaaaa tgtgcccaag cacgtgtggg 660

```
aagcgggcgt gcaccgagaa caatgagtgc tgccaccccg agtgcctggg cagctgcagc 720
gcgcctgaca acgacacggc ctgtgtagct tgccgccact actactatgc cggtgtctgt 780
gtgcctgcct gcccgcccaa cacctacagg tttgagggct ggcgctgtgt ggaccgtgac 840
ttctgcgcca acatcctcag cgccgagagc agcgactccg aggggtttgt gatccacgac 900
ggcgagtgca tgcaggagtg cccctcgggc ttcatccgca acggcagcca gagcatgtac 960
tgcatccctt gtgaaggtcc ttgcccgaag gtctgtgagg aagaaaagaa aacaaagacc 1020
attgattctg ttacttctgc tcagatgctc caaggatgca ccatcttcaa gggcaatttg 1080
ctcattaaca tccgacgggg gaataacatt gcttcagagc tggagaactt catggggctc 1140
atcgaggtgg tgacgggcta cgtgaagatc cgccattctc atgccttggt ctccttgtcc 1200
ttcctaaaaa accttcgcct catcctagga gaggagcagc tagaaggtgaa ttactccttc 1260
tacgtcctcg acaaccagaa cttgcagcaa ctgtgggact gggaccaccg caacctgacc 1320
atcaaagcag ggaaaatgta ctttgctttc aatcccaaat tatgtgtttc cgaaatttac 1380
cgcatggagg aagtgacggg gactaaaggg cgccaaagca aaggggacat aaacaccagg 1440
aacaacgggg agagagcctc ctgtgaaagt gacgtcctgc atttcacctc caccaccacg 1500
tcgaagaatc gcatcatcat aacctggcac cggtaccggc cccctgacta cagggatctc 1560
atcagcttca ccgtttacta caaggaagca ccctttaaga atgtcacaga gtatgatggg 1620
caggatgcct gcggctccaa cagctggaac atggtggacg tggacctccc gcccaacaag 1680
gacgtggagc ccggcatctt actacatggg ctgaagccct ggactcagta cgccgtttac 1740
gtcaaggctg tgaccctcac catggtggag aacgaccata tccgtggggc caagagtgag 1800
atcttgtaca ttcgcaccaa tgcttcagtt ccttccattc ccttggacgt tctttcagca 1860
tcgaactcct cttctcagtt aatcgtgaag tggaaccctc cctctctgcc caacggcaac 1920
ctgagttact acattgtgcg ctggcagcgg cagcctcagg acggctacct ttaccggcac 1980
aattactgct ccaaagacaa aatccccatc aggaagtatg ccgacggcac catcgacatt 2040
gaggaggtca cagagaaccc caagactgag gtgtgtggtg gggagaaagg gccttgctgc 2100
gcctgcccca aaactgaagc cgagaagcag gccgagaagg aggaggctga ataccgcaaa 2160
gtctttgaga atttcctgca caactccatc ttcgtgccca gacctgaaag gaagcggaga 2220
gatgtcatgc aagtggccaa caccaccatg tccagccgaa gcaggaacac cacggccgca 2280
gacacctaca acatcaccga cccggaagag ctggagacag agtaccctct ctttgagagc 2340
agagtggata acaaggagag aactgtcatt tctaaccttc ggcctttcac attgtaccgc 2400
atcgatatcc acagctgcaa ccacgaggct gagaagctgg gctgcagcgc ctccaactc 2460
gtctttgcaa ggactatgcc cgcagaagga gcagatgaca ttcctgggcc agtgacctgg 2520
gagccaaggc ctgaaaactc catctttttta aagtggccgg aacctgagaa tcccaatgga 2580
ttgattctaa tgtatgaaat aaaatacgga tcacaagttg aggatcagcg agaatgtgtg 2640
tccagacagg aatacaggaa gtatggaggg gccaagctaa accggctaaa cccggggaac 2700
tacacagccc ggattcaggc cacatctctc tctgggaatg ggtcgtggac agatcctgtg 2760
ttctttctatg tccaggccaa aacaggatat gaaaacttca tccatctgat catcgctctg 2820
cccgtcgctg tcctgttgat cgtgggaggg ttggtgatta tgctgtacgt cttccataga 2880
aagagaaata acagcaggct ggggaatgga gtgctgtatg ccttctgtgaa cccggagtac 2940
ttcagcgctg ctgatgtgta cgttcctgat gagtgggagg tggctcggga gaagatcacc 3000
atgagccggg aacttgggca ggggtcgttt ggagatggtct atgaaggagt tgccaagggt 3060
gtggtgaaag atgaacctga aaccagagtg gccattaaaa cagtgaacga ggccgcaagc 3120
atgcgtgaga ggattgagtt tctcaacgaa gcttctgtga tgaaggagtt caattgtcac 3180
catgtggtgc ggattgctgg tgtggtgtcc caaggccagc caacactggt catcatggaa 3240
ctgatgacac ggggcgatct caaaagttat ctccggtctc tgaggccaga aatggagaat 3300
aatccagtcc tagcacctcc aagcctgagc aagatgattc agatggccgg agagattgca 3360
gacggcatgg catacctcaa cgccaataag ttcgtccaca gagaccttgc tgcccggaat 3420
tgcatggtag ccgaagattt cacagtcaaa atcggagatt ttggtatgac gcgagatatc 3480
tatgagacag actattaccg gaaaggaggc aaagggctgc tgcccgtgcg ctggatgtct 3540
cctgagtccc tcaaggatgg agtcttccacc acttactcgg acgtctggtc cttcggggtc 3600
gtcctcttgg agatcgccac actggccgag cagccctacc agggcttgtc caacggagaa 3660
gtcctctggct tcgtcatgga gggcggcctt ctggacaagc cagacaactg tcctgacatg 3720
ctgtttgaac tgatgcggat gtgctggcag tataacccca agatgaggcc ttccttcctg 3780
gagatcatca gcagcatcaa agaggagatg gagcctggct tccgggaggt ctccttctac 3840
tacagcgagg agaacaagct gcccgagccg gaggagctgg acctggagcc agagaacatg 3900
gagagcgtcc ccctggaccc ctcggcctcc tcgtcctccc tgccactgcc cgacagacac 3960
tcaggacaca aggccgagaa cggccccggc cctgggggtgc tggtcctccg cgccagcttc 4020
gacgagagac agccttacgc ccacatgaac gggggccgca agaacgagcg ggccttgccg 4080
ctgccccagt cttcgacctg ctga                                        4104
```

<210> 92
<211> 726
<212> DNA
<213> Homo sapiens

<300>
<302> PDGFB
<310> NM002608

<400> 92
atgaatcgct gctgggcgct cttcctgtct ctctgctgct acctgcgtct ggtcagcgcc 60
gagggggacc ccattcccga ggagctttat gagatgctga gtgaccactc gatccgctcc 120
tttgatgatc tccaacgcct gctgcacgga gaccccggag aggaagatgg ggccgagttg 180
gacctgaaca tgacccgctc ccactctgga ggcgagctgg agagcttggc tcgtggaaga 240
aggagcctgg gttccctgac cattgctgag ccggccatga tcgccgagtg caagacgcgc 300
accgaggtgt tcgagatctc ccggcgcctc atagaccgca ccaacgccaa cttcctggtg 360
tggccgccct gtgtggaggt gcagcgctgc tccggctgct gcaacaaccg caacgtgcag 420
tgccgcccca cccaggtgca gctgcgacct gtccaggtga gaaagatcga gattgtgcgg 480
aagaagccaa tctttaagaa ggccacggtg acgctggaag accacctggc atgcaagtgt 540
gagacagtgg cagctgcacg gcctgtgacc cgaagcccgg ggggttccca ggagcagcga 600
gccaaaacgc cccaaactcg ggtgaccatt cggacggtgc gagtccgccg gcccccaag 660
ggcaagcacc ggaaattcaa gcacacgcat gacaagacgg cactgaagga gaccctgga 720
gcctag 726

<210> 93
<211> 1512
<212> DNA
<213> Homo sapiens

<300>
<302> TGFbetaR1
<310> NM004612

<400> 93
atggaggcgg cggtcgctgc tccgcgtccc cggctgctcc tcctcgtgct ggcggcggcg 60
gcggcggcgg cggcggcgct gctcccgggg gcgacggcgt tacagtgttt ctgccacctc 120
tgtacaaaag acaatttac ttgtgtgaca gatgggctct gctttgtctc tgtcacagag 180
accacagaca aagttataca caacagcatg tgtatagctg aaattgactt aattcctcga 240
gataggcegt ttgtatgtgc accctcttca aaaactgggt ctgtgactac aacatattgc 300
tgcaatcagg accattgcaa taaaatagaa cttccaacta ctgtaaagtc atcacctggc 360
cttggtcctg tggaactggc agctgtcatt gctggaccag tgtgcttcgt ctgcatctca 420
ctcatgttga tggtctatat ctgccacaac cgcactgtca ttcaccatcg agtgccaaat 480
gaagaggacc cttcattaga tcgccctttt atttcagagg gtactacgtt gaaagactta 540
atttatgata tgacaacgtc aggttctggc tcaggtttac cattgcttgt tcagagaaca 600
attgcgagaa ctattgtgtt acaagaaagc attggcaaag gtcgatttgg agaagtttgg 660
agaggaaagt ggcggggaga agaagttgct gttaagatat tctcctctag agaagaacgt 720
tcgtggttcc gtgaggcaga gatttatcaa actgtaatgt tacgtcatga aaacatcctg 780
ggatttatag cagcagacaa taaagacaat ggtacttgga ctcagctctg gttggtgtca 840
gattatcatg agcatggatc ccttttgat tacttaaaca gatacacagt tactgtggaa 900
ggaatgataa aacttgctct gtccacggcg agcggtcttg cccatcttca catggagatt 960
gttggtaccc aaggaaagcc agccattgct catagagatt tgaaatcaaa gaatatcttg 1020
gtaaagaaga atggaacttg ctgtattgca gacttaggac tggcagtaag acatgattca 1080
gccacagata ccattgatat tgctccaaac cacagagtgg gaacaaaaag gtacatggcc 1140
cctgaagttc tcgatgattc catgaatatg aaacatttg aatccttcaa acgtgctgac 1200
atctatgcaa tgggcttagt attctgggaa attgctcgac gatgttccat tggtggaatt 1260
catgaagatt accaactgcc ttattatgat cttgtacctt ctgacccatc agttgaagaa 1320
atgagaaaag ttgtttgtga acagaagtta aggccaaata tcccaaacag atggcagagc 1380
tgtgaagcct tgagagtaat ggctaaaatt atgagagaat gttggtatgc caatggagca 1440
gctaggctta cagcattgcg gattaagaaa acattatcgc aactcagtca acaggaaggc 1500

atcaaaatgt aa 1512

<210> 94
<211> 4044
<212> DNA
<213> Homo sapiens

<300>
<302> Flk1
<310> AF035121

<400> 94
atgcagagca aggtgctgct ggccgtcgcc ctgtggctct gcgtggagac ccgggccgcc 60
tctgtgggtt tgcctagtgt ttctcttgat ctgcccaggc tcagcataca aaaagacata 120
cttacaatta aggctaatac aactcttcaa attacttgca ggggacagag ggacttggac 180
tggctttggc ccaataatca gagtggcagt gagcaaaggg tggaggtgac tgagtgcagc 240
gatggcctct tctgtaagac actcacaatt ccaaaagtga tcggaaatga cactggagcc 300
tacaagtgct tctaccggga aactgacttg gcctcggtca tttatgtcta tgttcaagat 360
tacagatctc catttattgc ttctgttagt gaccaacatg gagtcgtgta cattactgag 420
aacaaaaaca aaactgtggt gattccatgt ctcgggtcca tttcaaatct caacgtgtca 480
ctttgtgcaa gatacccaga aaagagattt gttcctgatg gtaacagaat ttcctgggac 540
agcaagaagg gctttactat tcccagctac atgatcagct atgctggcat ggtcttctgt 600
gaagcaaaaa ttaatgatga aagttaccag tctattatgt acatagttgt cgttgtaggg 660
tataggattt atgatgtggt tctgagtccg tctcatggaa ttgaactatc tgttggagaa 720
aagcttgtct taaattgtac agcaagaact gaactaaatg tggggattga cttcaactgg 780
gaatacctt cttcgaagca tcagcataag aaacttgtaa accgagacct aaaaacccag 840
tctgggagtg agatgaagaa atttttgagc accttaacta tagatggtgt aacccggagt 900
gaccaaggat tgtacacctg tgcagcatcc agtgggctga tgaccaagaa gaacagcaca 960
tttgtcaggg tccatgaaaa acctttgtgt gcttttggaa gtggcatgga atctctggtg 1020
gaagccacgg tgggggagcg tgtcagaatc cctgcgaagt accttggtta cccacccca 1080
gaaataaaat ggtataaaaa tggaatacc cttgagtcca atcacacaat taaagcgggg 1140
catgtactga cgattatgga agtgagtgaa agagacacag gaaattacac tgtcatcctt 1200
accaatccca tttcaaagga gaagcagagc catgtggtct ctctggttgt gtatgtccca 1260
ccccagattg gtgagaaatc tctaatctct cctgtggatt cctaccagta cggcaccact 1320
caaacgctga catgtacggt ctatgccatt cctcccccgc atcacatcca ctggtattgg 1380
cagttggagg aagagtgcgc caacgagccc agccaagctg tctcagtgac aaacccatac 1440
ccttgtgaag aatggagaag tgtggaggac ttccaggggag gaaataaaat tgaagttaat 1500
aaaaatcaat ttgctctaat tgaaggaaaa aacaaaactg taagtaccct tgttatccaa 1560
gcggcaaatg tgtcagcttt gtacaaatgt gaagcggtca acaaagtcgg gagaggagag 1620
agggtgatct ccttccacgt gaccaggggt cctgaaatta ctttgcaacc tgacatgcag 1680
cccactgagc aggagagcgt gtctttgtgg tgcactgcag acagatctac gtttgagaac 1740
ctcacatggt acaagcttgg cccacagcct ctgccaatcc atgtgggaga gttgcccaca 1800
cctgtttgca agaacttgga tactctttgg aaattgaatg ccaccatgtt ctctaatagc 1860
acaaatgaca ttttgatcat ggagcttaag aatgcatcct tgcaggacca aggagactat 1920
gtctgccttg ctcaagacag gaagaccaag aaaagacatt gcgtggtcag gcagctcaca 1980
gtcctagagc gtgtggcacc cacgatcaca ggaaacctgg agaatcagac gacaagtatt 2040
ggggaaagca tcgaagtctc atgcacggca tctgggaatc cccctccaca gatcatgtgg 2100
tttaaagata atgagaccct tgtagaagac tcaggcattg tattgaagga tgggaaccgg 2160
aacctcacta tccgcagagt gaggaaggag gacgaaggcc tctacacctg ccaggcatgc 2220
agtgttcttg gctgtgcaaa agtggaggca ttttctataa tagaaggtgc ccaggaaaag 2280
acgaacttgg aaatcattat tctagtaggc acggcggtga ttgccatgtt cttctggcta 2340
cttcttgtca tcatcctacg gaccgttaag cgggccaatg gaggggaact gaagacaggc 2400
tacttgtcca tcgtcatgga tccagatgaa ctcccattgg atgaacattg tgaacgactg 2460
ccttatgatg ccagcaaatg ggaattcccc agagaccggc tgaagctagg taagcctctt 2520
ggccgtggtg cctttggcca agtgattgaa gcagatgcct ttggaattga caagacagca 2580
acttgcagga cagtagcagt caaaatgttg aaagaaggag caacacacag tgagcatcga 2640
gctctcatgt ctgaactcaa gatcctcatt catattggtc accatctcaa tgtggtcaac 2700
cttctaggtg cctgtaccaa gccaggaggg ccactcatgg tgattgtgga atttctgcaaa 2760
tttggaaacc tgtccactta cctgaggagc aagagaaatg aatttgtccc ctacaagacc 2820

aaaggggcac gattccgtca agggaaagac tacgttggag caatccctgt ggatctgaaa 2880
cggcgcttgg acagcatcac cagtagccag agctcagcca gctctggatt tgtggaggag 2940
aagtccctca gtgatgtaga agaagaggaa gctcctgaag atctgtataa ggacttcctg 3000
accttggagc atctcatctg ttacagcttc caagtggcta agggcatgga gttcttggca 3060
tcgcgaaagt gtatccacag ggacctggcg gcacgaaata tcctcttatc ggagaagaac 3120
gtggttaaaa tctgtgactt tggcttggcc cgggatattt ataaagatcc agattatgtc 3180
agaaaaggag atgctcgcct ccctttgaaa tggatggccc cagaaacaat ttttgacaga 3240
gtgtacacaa tccagagtga cgtctggtct tttggtgttt tgctgtggga aatattttcc 3300
ttaggtgctt ctccatatcc tggggtaaag attgatgaag aattttgtag gcgattgaaa 3360
gaaggaacta gaatgagggc ccctgattat actacacccag aaatgtacca gaccatgctg 3420
gactgctggc acggggagcc cagtcagaga cccacgtttt cagagttggt ggaacatttg 3480
ggaaatctct tgcaagctaa tgctcagcag gatggcaaag actacattgt tcttccgata 3540
tcagagactt tgagcatgga agaggattct ggactctctc tgcctacctc acctgtttcc 3600
tgtatggagg aggaggaagt atgtgacccc aaattccatt atgacaacac agcaggaatc 3660
agtcagtatc tgcagaacag taagcgaaag agccggcctg tgagtgtaaa aacatttgaa 3720
gatatcccgt tagaagaacc agaagtaaaa gtaatcccag atgacaacca gacggacagt 3780
ggtatggttc ttgcctcaga agagctgaaa actttggaag acagaaccaa attatctcca 3840
tcttttggtg gaatggtgcc cagcaaaagc agggagtctg tggcatctga aggctcaaac 3900
cagacaagcg gctaccagtc cggatatcac tccgatgaca cagacaccac cgtgtactcc 3960
agtgaggaag cagaactttt aaagctgata gagattggag tgcaaaccgg tagcacagcc 4020
cagattctcc agcctgactc gggg 4044

<210> 95
<211> 4017
<212> DNA
<213> Homo sapiens

<300>
<302> Flt1
<310> AF063657

<400> 95
atggtcagct actgggacac cggggtcctg ctgtgcgcgc tgctcagctg tctgcttctc 60
acaggatcta gttcaggttc aaaatttaaaa gatcctgaac tgagtttaaa aggcacccag 120
cacatcatgc aagcaggcca gacactgcat ctccaatgca gggggagagc agcccataaa 180
tggtctttgc ctgaaatggt gagtaaggaa agcgaaaggc tgagcataac taaatctgcc 240
tgtggaagaa atggcaaaca attctgcagt actttaacct tgaacacagc tcaagcaaac 300
cacactggct tctacagctg caaatatcta gctgtaccta cttcaaagaa gaaggaaaca 360
gaatctgcaa tctatatatt tattagtgat acaggtagac ctttcgtaga gatgtacagt 420
gaaatccccg aaattataca catgactgaa ggaaggagc tcgtcattcc ctgccgggtt 480
acgtcaccta acatcactgt tactttaaaa aagtttccac ttgacacttt gatccctgat 540
ggaaaacgca taatctggga cagtagaaag ggcttcatca tatcaaatgc aacgtacaaa 600
gaaatagggc ttctgacctg tgaagcaaca gtcaatgggc atttgtataa gacaaactat 660
ctcacacatc gacaaaccaa tacaatcata gatgtccaaa taagcacacc acgcccagtc 720
aaattactta gaggccatac tcttgtcctc aattgtactg ctaccactcc cttgaacacg 780
agagttcaaa tgacctggag ttaccctgat gaaaaaaata agagagcttc cgtaaggcga 840
cgaattgacc aaagcaattc ccatgccaac atattctaca gtgttcttac tattgacaaa 900
atgcagaaca aagacaaagg actttatact tgtcgtgtaa ggagtggacc atcattcaaa 960
tctgttaaca cctcagtgca tatatatgat aaagcattca tcactgtgaa acatcgaaaa 1020
cagcaggtgc ttgaaaccgt agctggcaag cggtcttacc ggctctctat gaaagtgaag 1080
gcatttccct cgccggaagt tgtatggtta aaagatgggt tacctgcgac tgagaaatct 1140
gctcgctatt tgactctgtg ctactcgtta attatcaagg acgtaactga agaggatgca 1200
gggaattata caatcttgct gagcataaaa cagtcaaatg tgtttaaaaa cctcactgcc 1260
actctaattg tcaatgtgaa accccagatt taccgaaaagg ccgtgtcatc gtttccagac 1320
ccggctctct acccactggg cagcagacaa atcctgactt gtaccgcata tggtatccct 1380
caacctacaa tcaagtggtt ctggcacccc tgtaaccata atcattccga agcaaggtgt 1440
gacttttgtt ccaataatga agagtccttt atcctggatg ctgacagcaa catgggaaac 1500
agaattgaga gcatcactca gcgcatggca ataatagaag gaaagaatag gatggctagc 1560
accttggttg tggctgactc tagaatttct ggaatctaca tttgcatagc ttccaataaa 1620

gttgggactg tgggaagaaa cataagcttt tatatcacag atgtgccaaa tgggtttcat 1680
gttaacttgg aaaaaatgcc gacggaagga gaggacctga aactgtcttg cacagttaac 1740
aagttcttat acagagacgt tacttggatt ttactgcgga cagttaataa cagaacaatg 1800
cactacagta ttagcaagca aaaaatggcc atcactaagg agcactccat cactcttaat 1860
cttaccatca tgaatgtttc cctgcaagat tcaggcacct atgcctgcag agccaggaat 1920
gtatacacag gggaagaaat cctccagaag aaagaaatta caatcagaga tcaggaagca 1980
ccatacctcc tgcgaaacct cagtgatcac acagtggcca tcagcagttc caccacttta 2040
gactgtcatg ctaatggtgt ccccgagcct cagatcactt ggtttaaaaa caaccacaaa 2100
atacaacaag agcctggaat tattttagga ccaggaagca gcacgctgtt tattgaaaga 2160
gtcacagaag aggatgaagg tgtctatcac tgcaaagcca ccaaccagaa gggctctgtg 2220
gaaagttcag catacctcac tgttcaagga acctcggaca agtctaatct ggagctgatc 2280
actctaacat gcacctgtgt ggctgcgact ctctttctggc tcctattaac cctctttatc 2340
cgaaaaatga aaaggtcttc ttctgaaata aagactgact acctatcaat tataatggac 2400
ccagatgaag ttcctttgga tgagcagtgt gagcggctcc cttatgatgc cagcaagtgg 2460
gagtttgccc gggagagact taaactgggc aaatcacttg gaagaggggc ttttggaaaa 2520
gtggttcaag catcagcatt tggcattaag aaatcaccta cgtgccggac tgtggctgtg 2580
aaaatgctga aagagggggc cacggccagc gagtacaaag ctctgatgac tgagctaaaa 2640
atcttgaccc acattggcca ccatctgaac gtggttaacc tgctgggagc ctgcaccaag 2700
caaggagggc ctctgatggt gattgttgaa tactgcaaat atggaaatct ctccaactac 2760
ctcaagagca aacgtgactt atttttctc aacaaggatg cagcactaca catggagcct 2820
aagaaagaaa aaatggagcc aggcctggaa caaggcaaga aaccaagact agatagcgtc 2880
accagcagcg aaagctttgc gagctccggc tttcaggaag ataaaagtct gagtgatgtt 2940
gaggaagagg aggattctga cggtttctac aaggagccca tcactatgga agatctgatt 3000
tcttacagtt ttcaagtggc cagaggcatg gagttcctgt cttccagaaa gtgcattcat 3060
cgggacctgg cagcgagaaa cattctttta tctgagaaca acgtggtgaa gatttgtgat 3120
tttggccttg cccgggatat ttataagaac cccgattatg tgagaaaagg agtactcga 3180
cttcctctga aatggatggc tcctgaatct atctttgaca aaatctacag caccaagagc 3240
gacgtgtggt cttacggagt attgctgtgg gaaatcttct ccttaggtgg gtctccatac 3300
ccaggagtac aaatggatga ggacttttgc agtcgcctga gggaaggcat gaggatgaga 3360
gctcctgagt actctactcc tgaaatctat cagatcatgc tggactgctg gcacagagac 3420
ccaaaagaaa ggccaagatt tgcagaactt gtggaaaaac taggtgattt gcttcaagca 3480
aatgtacaac aggatggtaa agactacatc ccaatcaatg ccatactgac aggaaatagt 3540
gggtttacat actcaactcc tgccttctct gaggacttct tcaaggaaag tatttcagct 3600
ccgaagttta attcaggaag ctctgatgat gtcagatatg taaatgcttt caagttcatg 3660
agcctggaaa gaatcaaaac ctttgaagaa cttttaccga atgccacctc catgtttgat 3720
gactaccagg gcgacagcag cactctgttg gcctctccca tgctgaagcg cttcacctgg 3780
actgacagca aacccaaggc ctcgctcaag attgacttga gagtaaccag taaaagtaag 3840
gagtcggggc tgtctgatgt cagcaggccc agtttctgcc attccagctg tgggcacgtc 3900
agcgaaggca agcgcaggtt cacctacgac cacgctgagc tggaaaggaa aatcgcgtgc 3960
tgctccccgc ccccagacta caactcggtg gtcctgtact ccaccccacc catctag 4017

<210> 96
<211> 3897
<212> DNA
<213> Homo sapiens

<300>
<302> Flt4
<310> XM003852

<400> 96
atgcagcggg gcgccgcgct gtgcctgcga ctgtggctct gcctgggact cctggacggc 60
ctggtgagtg gctactccat gaccccccg accttgaaca tcacggagga gtcacacgtc 120
atcgacaccg gtgacagcct gtccatctcc tgcagggggac agcaccccct cgagtgggct 180
tggccaggag ctcaggaggc gccagccacc ggagacaagg acagcgagga cacgggggtg 240
gtgcgagact gcgagggcac agacgccagg ccctactgca aggtgttgct gctgacgag 300
gtacatgcca acgacacagg cagctacgtc tgctactaca agtacatcaa ggcacgcatc 360
gagggcacca cggccgccag ctcctacgtg ttcgtgagag actttgagca gccattcatc 420
aacaagcctg acacgctctt ggtcaacagg aaggacgcca tgtgggtgcc ctgtctggtg 480

tccatccccg gcctcaatgt cacgctgcgc tcgcaaagct cggtgctgtg gccagacggg 540
caggaggtgg tgtgggatga ccggcggggc atgctcgtgt ccacgccact gctgcacgat 600
gccctgtacc tgcagtgcga gaccacctgg ggagaccagg acttcctttc caaccccttc 660
ctggtgcaca tcacaggcaa cgagctctat gacatccagc tgttgcccag gaagtcggtg 720
gagctgctgg taggggagaa gctggtcctg aactgcaccg tgtgggctga gtttaactca 780
ggtgtcacct ttgactggga ctacccaggg aagcaggcag agcgggggtaa gtgggtgccc 840
gagcgacgct cccagcagac ccacacagaa ctctccagca tcctgaccat ccacaacgtc 900
agccagcacg acctgggctc gtatgtgtgc aaggccaaca acggcatcca gcgatttcgg 960
gagagcaccg aggtcattgt gcatgaaaat cccttcatca gcgtcgagtg gctcaaagga 1020
cccatcctgg aggccacggc aggagacgag ctggtgaagc tgcccgtgaa gctggcagcg 1080
taccccccgc ccgagttcca gtggtacaag gatggaaagg cactgtccgg gcgccacagt 1140
ccacatgccc tggtgctcaa ggaggtgaca gaggccagca caggcaccta cacctcgcc 1200
ctgtggaact ccgctgctgg cctgaggcgc aacatcagcc tggagctggt ggtgaatgtg 1260
ccccccacga tacatgagaa ggaggcctcc tccccagca tctactcgcg tcacagccgc 1320
caggccctca cctgcacggc ctacggggtg cccctgcctc tcagcatcca gtggcactgg 1380
cggccctgga caccctgcaa gatgtttgcc cagcgtagtc tccggcggcg gcagcagcaa 1440
gacctcatgc cacagtgccg tgactggagg gcggtgaccg cgcaggatgc cgtgaacccc 1500
atcgagagcc tggacacctg gaccgagttt gtggaggggaa agaataagac tgtgagcaag 1560
ctggtgatcc agaatgccaa cgtgtctgcc atgtacaagt gtgtggtctc caacaaggtg 1620
ggccaggatg agcggctcat ctacttctat gtgaccacca tccccgacgg cttcaccatc 1680
gaatccaagc catccgagga gctactagag ggccagccgg tgctcctgag ctgccaagcc 1740
gacagctaca agtacgagca tctgcgctgg taccgcctca acctgtccac gctgcacgat 1800
gcgcacggga accegcttct gctcgactgc aagaacgtgc atctgttcgc caccccctctg 1860
gccgccagcc tggaggaggt ggcacctggg gcgccgccacg ccacgctcag cctgagtatc 1920
ccccgctcg cgcccgagca cgagggccac tatgtgtgcg aagtgcaaga ccggcgcagc 1980
catgacaagc actgccacaa gaagtacctg tcggtgcagg ccctggaagc ccctcggctc 2040
acgcagaact tgaccgacct cctggtgaac gtgagcgact cgctggagat gcagtgcttg 2100
gtggccggag cgcacgcgcc cagcatcgtg tggtacaaag acgagaggct gctggaggaa 2160
aagtctggag tcgacttggc ggactccaac cagaagctga gcatccagcg cgtgcgcgag 2220
gaggatgcgg gacgctatct gtgcagcgtg tgcaacgcca agggctgcgt caactcctcc 2280
gccagcgtgg ccgtggaagg ctccgaggat aaggqcagca tggagatcgt gatccttgtc 2340
ggtaccggcg tcatcgctgt cttcttctgg gtcctcctcc tcctcatctt ctgtaacatg 2400
aggaggccgg cccacgcaga catcaagacg ggctacctgt ccatcatcat ggaccccggg 2460
gaggtgcctc tggaggagca atgcgaatac ctgtcctacg atgccagcca gtgggaattc 2520
ccccgagagc ggctgcacct ggggagagtg ctcggctacg gcgcctttcgg gaaggtggtg 2580
gaagcctccg ctttcggcat ccacaagggc agcagctgtg acaccgtggc cgtgaaaatg 2640
ctgaaagagg gcgccacggc cagcgagcag cgcgcgctga tgtcggagct caagatcctc 2700
attcacatcg gcaacctcct caacgtggtc aacctcctcg gggcgtgcac caagccgcag 2760
ggccccctca tggtgatcgt ggagttctgc aagtacggca acctctccaa cttcctgcgc 2820
gccaagcggg acgccttcag ccccgcgcg gagaagtctc ccgagcagcg cggacgcttc 2880
cgcgccatgg tggagctcgc caggctggat cggaggcggc cggggagcag cgacagggtc 2940
ctcttcgcgc ggttctcgaa gaccgagggc ggagcgaggc gggcttctcc agaccaagaa 3000
gctgaggacc tgtggctgag cccgctgacc atggaagatc ttgtctgcta cagcttccag 3060
gtggccagag ggatggagtt cctggcttcc cgaaagtgca tccacagaga tctgcgtgct 3120
cggaacattc tgctgtcgga aagcgacgtg gtgaagatct gtgactttgg ccttgcccgg 3180
gacatctaca aagaccccga ctacgtccgc aagggcagtg cccggctgcc cctgaagtgg 3240
atggccctg aaagcatctt cgacaaggtg tacaccacgc agagtgacgt gtggtccttt 3300
ggggtgttc tctggagat cttctctg ggggcctcc cgtacctgg ggtgcagatc 3360
aatgaggagt tctgccagcg gctgagagac ggcacaagga tgagggccc ggagctggcc 3420
actcccgcca tacgccgcat catgctgaac tgctggtccg gagacccaa ggcgagacct 3480
gcattctcgg agctggtgga gatcctgggg gacctgctcc agggcagggg cctgcaagag 3540
gaagaggagg tctgcatggc cccgcgcagc tctcagagct cagaagaggg cagcttctcg 3600
caggtgtcca ccatggccct acacatcgcc caggctgacg ctgaggacag cccgccaagc 3660
ctgcagcgcc acagcctggc cgccaggtat tacaactggg tgtcctttcc cgggtgcctg 3720
gccagaggag ctgagacccg tggttcctcc aggatgaaga catttgagga attcccccatg 3780
accccaacga cctacaaagg ctctgtggac aaccagacag acagtgggat ggtgctggcc 3840
tcggaggagt ttgagcagat agagagcagg catagacaag aaagcggctt caggtag 3897

<210> 97

<211> 4071
<212> DNA
<213> Homo sapiens

<300>
<302> KDR
<310> AF063658

<400> 97
atggagagca aggtgctgct ggccgtcgcc ctgtggctct gcgtggagac ccgggccgcc 60
tctgtgggtt tgcctagtgt ttctcttgat ctgccccaggc tcagcataca aaaagacata 120
cttacaatta aggctaatac aactcttcaa attacttgca ggggacagag ggacttggac 180
tggcttttggc ccaataatca gagtggcagt gagcaaaggg tggaggtgac tgagtgcagc 240
gatggcctct tctgtaagac actcacaatt ccaaaagtga tcggaaatga cactggagcc 300
tacaagtgct tctaccggga aactgacttg gcctcggtca tttatgtcta tgttcaagat 360
tacagatctc catttattgc ttctgttagt gaccaacatg gagtcgtgta cattactgag 420
aacaaaaaca aaactgtggt gattccatgt ctcgggtcca tttcaaatct caacgtgtca 480
ctttgtgcaa gatacccaga aaagagattt gttcctgatg gtaacagaat ttcctgggac 540
agcaagaagg gctttactat tcccagctac atgatcagct atgctggcat ggtcttctgt 600
gaagcaaaaa ttaatgatga aagttaccag tctattatgt acatagttgt cgttgtaggg 660
tataggattt atgatgtggt tctgagtccg tctcatggaa ttgaactatc tgttggagaa 720
aagcttgtct taaattgtac agcaagaact gaactaaatg tggggattga cttcaactgg 780
gaataccctt cttcgaagca tcagcataag aaacttgtaa accgagacct aaaaacccag 840
tctgggagtg agatgaagaa atttttgagc accttaacta tagatggtgt aacccggagt 900
gaccaaggat tgtacacctg tgcagcatcc agtgggctga tgaccaagaa gaacagcaca 960
tttgtcaggg tccatgaaaa acctttttgtt gcttttggaa gtggcatgga atctctggtg 1020
gaagccacgg tgggggagcg tgtcagaatc cctgcgaagt accttggtta cccacccca 1080
gaaataaaat ggtataaaaa tggaatacc cttgagtcca atcacacaat taaagcgggg 1140
catgtactga cgattatgga agtgagtgaa agagacacag gaaattacac tgtcatcctt 1200
accaatccca tttcaaagga gaagcagagc catgtggtct ctctggttgt gtatgtccca 1260
ccccagattg gtgagaaatc tctaatctct cctgtggatt cctaccagta cggcaccact 1320
caaacgctga catgtacggt ctatgccatt cctcccccgc atcacatcca ctggtattgg 1380
cagttggagg aagagtgcgc caacgagccc agccaagctg tctcagtgac aaacccatac 1440
ccttgtgaag aatggagaag tgtggaggac ttccagggag gaaataaaat tgaagttaat 1500
aaaaatcaat ttgctctaat tgaaggaaaa aacaaaactg taagtaccct tgttatccaa 1560
gcggcaaatg tgtcagcttt gtacaaatgt gaagcggtca acaaagtcgg gagaggagag 1620
agggtgatct ccttccacgt gaccaggggt cctgaaatta ctttgcaacc tgacatgcag 1680
cccactgagc aggagagcgt gtctttgtgg tgcactgcag acagatctac gtttgagaac 1740
ctcacatggt acaagcttgg cccacagcct ctgccaatcc atgtgggaga gttgcccaca 1800
cctgtttgca agaacttgga tactctttgg aaattgaatg ccaccatgtt ctctaatagc 1860
acaaatgaca ttttgatcat ggagcttaag aatgcatcct tgcaggacca aggagactat 1920
gtctgccttg ctcaagacag gaagaccaag aaaagacatt gcgtggtcag gcagctcaca 1980
gtcctagagc gtgtggcacc cacgatcaca ggaaacctgg agaatcagac gacaagtatt 2040
ggggaaagca tcgaagtctc atgcacggca tctgggaatc cccctccaca gatcatgtgg 2100
tttaaagata atgagaccct tgtagaagac tcaggcattg tattgaagga tgggaaccgg 2160
aacctcacta tccgcagagt gaggaaggag gacgaaggcc tctacacctg ccaggcatgc 2220
agtgttcttg gctgtgcaaa agtggaggca tttttcataa tagaaggtgc ccaggaaaag 2280
acgaacttgg aaatcattat tctagtaggc acggcggtga ttgccatgtt ctttctggcta 2340
cttcttgtca tcatcctacg gaccgttaag cgggccaatg gaggggaact gaagacaggc 2400
tacttgtcca tcgtcatgga tccagatgaa ctcccattgg atgaacattg tgaacgactg 2460
ccttatgatg ccagcaaatg ggaattcccc agagaccggc tgaagctagg taagcctctt 2520
ggccgtggtg cctttggcca agtgattgaa gcagatgcct ttggaattga cagacagca 2580
acttgcagga cagtagcagt caaaatgttg aaagaaggag caacacacag tgagcatcga 2640
gctctcatgt ctgaactcaa gatcctcatt catattggtc accatctcaa tgtggtcaac 2700
cttctaggtg cctgtaccaa gccaggaggg ccactcatgg tgattgtgga attctgcaaa 2760
tttggaaacc tgtccacttа cctgaggagc aagagaaatg aatttgtcc ctacaagacc 2820
aaaggggcac gattccgtca agggaaagac tacgttggag caatccctgt ggatctgaaa 2880
cggcgcttgg acagcatcac cagtagccag agctccagcca gctctggatt tgtggaggag 2940
aagtccctca gtgatgtaga agaagaggaa gctcctgaag atctgtataa ggacttcctg 3000
accttggagc atctcatctg ttacagcttc caagtggcta agggcatgga gttcttggca 3060

tcgcgaaagt gtatccacag ggacctggcg gcacgaaata tcctcttatc ggagaagaac 3120
gtggttaaaa tctgtgactt tggcttggcc cgggatattt ataaagatcc agattatgtc 3180
agaaaaggag atgctcgcct ccctttgaaa tggatggccc cagaaacaat ttttgacaga 3240
gtgtacacaa tccagagtga cgtctggtct tttggtgttt tgctgtggga aatattttcc 3300
ttaggtgctt ctccatatcc tggggtaaag attgatgaag aattttgtag gcgattgaaa 3360
gaaggaacta gaatgagggc ccctgattat actacaccag aaatgtacca gaccatgctg 3420
gactgctggc acgggggagcc cagtcagaga cccacgtttt cagagttggt ggaacatttg 3480
ggaaatctct tgcaagctaa tgctcagcag gatggcaaag actacattgt tcttccgata 3540
tcagagactt tgagcatgga agaggattct ggactctctc tgcctacctc acctgtttcc 3600
tgtatggagg aggaggaagt atgtgacccc aaattccatt atgacaacac agcaggaatc 3660
agtcagtatc tgcagaacag taagcgaaag agccggcctg tgagtgtaaa aacatttgaa 3720
gatatcccgt tagaagaacc agaagtaaaa gtaatcccag atgacaacca gacggacagt 3780
ggtatggttc ttgcctcaga agagctgaaa actttggaag acagaaccaa attatctcca 3840
tcttttggtg gaatggtgcc cagcaaaagc agggagtctg tggcatctga aggctcaaac 3900
cagacaagcg gctaccagtc cggatatcac tccgatgaca cagacaccac cgtgtactcc 3960
agtgaggaag cagaacttttaaagctgata gagattggag tgcaaaccgg tagcacagcc 4020
cagattctcc agcctgactc ggggaccaca ctgagctctc ctcctgttta a 4071

<210> 98
<211> 1410
<212> DNA
<213> Homo sapiens

<300>
<302> MMP1
<310> M13509

<400> 98
atgcacagct ttcctccact gctgctgctg ctgttctggg gtgtggtgtc tcacagcttc 60
ccagcgactc tagaaacaca agagcaagat gtggacttag tccagaaata cctggaaaaa 120
tactacaacc tgaagaatga tgggaggcaa gttgaaaagc ggagaaatag tggccagtg 180
gttgaaaaat tgaagcaaat gcaggaattc tttgggctga aagtgactgg gaaaccagat 240
gctgaaaccc tgaaggtgat gaagcagccc agatgtggag tgcctgatgt ggctcagttt 300
gtcctcactg agggaaaccc tcgctgggag caaacacatc tgaggtacag gattgaaaat 360
tacacgccag atttgccaag agcagatgtg gaccatgcca ttgagaaagc cttccaactc 420
tggagtaatg tcacacctct gacattcacc aaggtctctg agggtcaagc agacatcatg 480
atatcttttg tcaggggaga tcatcgggac aactctcctt ttgatggacc tggaggaaat 540
cttgctcatg cttttcaacc aggcccaggt attggagggg atgctcattt tgatgaagat 600
gaaaggtgga ccaacaattt cagagagtac aacttacatc gtgttgcggc tcatgaactc 660
ggccatttctc ttggactctc ccatttctact gatatcgggg ctttgatgta ccctagctac 720
accttcagtg gtgatgttca gctagctcag gatgacattg atggcatcca agccatatat 780
ggacgttccc aaaatcctgt ccagccccatc ggcccacaaa ccccaaaagc gtgtgacagt 840
aagctaacct ttgatgctat aactacgatt cggggagaag tgatgttctt taaagacaga 900
ttctacatgc gcacaaatcc cttctacccg gaagttgagc tcaatttcat ttctgttttc 960
tggccacaac tgccaaatgg gcttgaagct gcttacgaat ttgccgacag agatgaagtc 1020
cggtttttca aagggaataa gtactgggct gttcagggac agaatgtgct acacggatac 1080
cccaaggaca tctacagctc ctttggcttc cctagaactg tgaagcatat cgatgctgct 1140
ctttctgagg aaaacactgg aaaaacctac ttctttgttg ctaacaaata ctggaggtat 1200
gatgaatata aacgatctat ggatccaagt tatcccaaaa tgatagcaca tgacttttct 1260
ggaattggcc acaaagttga tgcagttttc atgaaagatg gattttttcta tttctttcat 1320
ggaacaagac aatacaaatt tgatcctaaa acgaagagaa ttttgactct ccagaaagct 1380
aatagctggt tcaactgcag gaaaaattga 1410

<210> 99
<211> 1743
<212> DNA
<213> Homo sapiens

<300>
<302> MMP10
<310> XM006269

<400> 99
aaagaaggta agggcagtga gaatgatgca tcttgcattc cttgtgctgt tgtgtctgcc 60
agtctgctct gcctatcctc tgagtggggc agcaaaagag gaggactcca acaaggatct 120
tgcccagcaa tacctagaaa agtactacaa cctcgaaaag gatgtgaaac agtttacatt 180
aaaggacagt aatctcattg ttaaaaaaat ccaaggaatg cagaagttcc ttgggttgga 240
ggtgacaggg aagctagaca ctgacactct ggaggtgatg cgcaagccca ggtgtggagt 300
tcctgacgtt ggtcacttca gctccttttcc tggcatgccg aagtggagga aaaccccact 360
tacatacagg attgtgaatt atacaccaga tttgccaaga gatgctgttg attctgccat 420
tgagaaagct ctgaaagtct gggaagaggt gactccactc acattctcca ggctgtatga 480
aggagaggct gatataatga tctcttttgc agttaaagaa catggagact tttactcttt 540
tgatggccca ggacacagtt tggctcatgc ctacccacct ggacctgggc tttatggaga 600
tattcacttt gatgatgatg aaaaatggac agaagatgca tcaggcacca atttattcct 660
cgttgctgct catgaacttg gccactccct ggggctcttt cactcagcca acactgaagc 720
tttgatgtac ccactctaca actcattcac agagctcgcc cagttccgcc tttcgcaaga 780
tgatgtgaat ggcattcagt ctctctacgg acctccccct gcctctactg aggaaccccct 840
ggtgcccaca aaatctgttc cttcgggatc tgagatgcca gccaagtgtg atcctgcttt 900
gtccttcgat gccatcagca ctctgagggg agaatatctg ttctttaaag acagatattt 960
ttggcgaaga tcccactgga accctgaacc tgaatttcat ttgatttctg catttggcc 1020
ctctcttcca tcatatttgg atgctgcata tgaagttaac agcagggaca ccgttttttat 1080
ttttaaagga aatgagttct gggccatcag aggaaatgag gtacaagcag gttatccaag 1140
aggcatccat accctgggtt ttcctccaac cataaggaaa attgatgcag ctgtttctga 1200
caaggaaaag aagaaaacat acttctttgc agcggacaaa tactggagat ttgatgaaaa 1260
tagccagtcc atggagcaag gcttccctag actaatagct gatgactttc caggagttga 1320
gcctaaggtt gatgctgtat tacaggcatt tggatttttc tacttcttca gtggatcatc 1380
acagtttgag tttgacccca atgccaggat ggtgacacac atattaaaga gtaacagctg 1440
gttacattgc taggcgagat aggggaaaga cagatatggg tgtttttaat aaatctaata 1500
attattcatc taatgtatta tgagccaaaa tggttaattt ttcctgcatg ttctgtgact 1560
gaagaagatg agccttgcag atatctgcat gtgtcatgaa ggaatgtttct ggaattcttc 1620
acttgctttt gaattgcact gaacagaatt aagaaatact catgtgcaat aggtgagaga 1680
atgtattttc atagatgtgt tattacttcc tcaataaaaa gttttatttt gggcctgttc 1740
ctt 1743

<210> 100
<211> 1467
<212> DNA
<213> Homo sapiens

<300>
<302> MMP11
<310> XM009873

<400> 100
atggctccgg ccgcctggct ccgcagcgcg gccgcgcgcg ccctcctgcc cccgatgctg 60
ctgctgctgc tccagccgcc gccgctgctg gcccgggctc tgccgccgga cgcccaccac 120
ctccatgccg agaggagggg gccacagccc tggcatgcag ccctgcccag tagcccggca 180
cctgcccctg ccacgcagga agccccccgg cctgccagca gcctcaggcc tccccgctgt 240
ggcgtgcccg acccatctga tgggctgagt gcccgcaacc gacagaagag gttcgtgctt 300
tctggcgggc gctgggagaa gacggacctc acctacagga tccttcggtt cccatggcag 360
ttggtgcagg agcaggtgcg gcagacgatg gcagaggccc taaaggtatg gagcgatgtg 420
acgccactca cctttactga ggtgcacgag ggccgtgctg acatcatgat cgacttcgcc 480
aggtactggc atgggacga cctgccgttt gatgggcctg ggggcatcct ggcccatgcc 540
ttcttcccca agactcaccg agaaggggat gtccacttcg actatatgatga gacctggact 600
atcgggatg accagggcac agacctgctg caggtggcag cccatgaatt tggccacgtg 660
ctggggctgc agcacacaac agcagccaag gccctgatgt ccgccttcta caccttttcgc 720
tacccactga gtctcagccc agatgactgc aggggcgttc aacacctata tggccagccc 780

tggcccactg tcacctccag gaccccagcc ctgggccccc aggctgggat agacaccaat 840
gagattgcac cgctggagcc agacgccccg ccagatgcct gtgaggcctc ctttgacgcg 900
gtctccacca tccgaggcga gctctttttc ttcaaagcgg gctttgtgtg gcgcctccgt 960
ggggccagc tgcagcccgg ctacccagca ttggcctctc gccactggca gggactgccc 1020
agccctgtgg acgctgcctt cgaggatgcc cagggccaca tttggttctt ccaaggtgct 1080
cagtactggg tgtacgacgg tgaaaagcca gtcctgggcc ccgcacccct caccgagctg 1140
ggcctggtga ggttcccggt ccatgctgcc ttggtctggg gtcccgagaa gaacaagatc 1200
tacttcttcc gaggcaggga ctactggcgt ttccacccca gcacccggcg tgtagacagt 1260
cccgtgcccc gcagggccac tgactggaga ggggtgccct ctgagatcga cgctgccttc 1320
caggatgctg atggctatgc ctacttcctg cgcggccgcc tctactggaa gtttgaccct 1380
gtgaaggtga aggcttcgga aggcttcccc cgtctcgtgg gtcctgactt ctttggctgt 1440
gccgagcctg ccaacacttt cctctga 1467

<210> 101
<211> 1653
<212> DNA
<213> Homo sapiens

<300>
<302> MMP12
<310> XM006272

<400> 101
atgaagtttc ttctaatact gctcctgcag gccactgctt ctggagctct tccctgaac 60
agctctacaa gcctggaaaa aaataatgtg ctatttggtg agagatactt agaaaaattt 120
tatggccttg agataaacaa acttccagtg acaaaaatga aatatagtgg aaacttaatg 180
aaggaaaaaa tccaagaaat gcagcacttc ttgggtctga aagtgaccgg gcaactggac 240
acatctaccc tggagatgat gcacgcacct cgatgtggag tccccgatgt ccatcatttc 300
agggaaatgc caggggggcc cgtatggagg aaacattata tcacctacag aatcaataat 360
tacacacctg acatgaaccg tgaggatgtt gactacgcaa tccggaaagc tttccaagta 420
tggagtaatg ttaccccctt gaaattcagc aagattaaca caggcatggc tgacattttg 480
gtggttttg cccgtggagc tcatggagac ttccatgctt ttgatggcaa aggtggaatc 540
ctagcccatg cttttggacc tggatctggc attggaggggg atgcacattt cgatgaggac 600
gaattctgga ctacacattc aggagnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 660
nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 720
nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 780
nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 840
nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn nnnnnnnnnn 900
nnnnnnnnnn nnnnnnnnnn nnnnngagag gatccaaagg ccgtaatgtt ccccacctac 960
aaatatgttg acatcaacac atttcgcctc tctgctgatg acatacgtgg cattcagtcc 1020
ctgtatggag acccaaaaga gaaccaacgc ttgccaaatc ctgacaattc agraccagct 1080
ctctgtgacc ccaatttgag ttttgatgct gtcactaccg tgggaaataa gatcttttttc 1140
ttcaaagaca ggttcttctg gctgaaggtt tctgagagac caaagaccag tgttaatttta 1200
atttcttcct tatggccaac cttgccatct ggcattgaag ctgcttatga aattgaagcc 1260
agaaatcaag ttttttcttt taaagatgac aaatactggt taattagcaa tttaagacca 1320
gagccaaatt atcccaagag catacattct tttggttttc ctaactttgt gaaaaaaatt 1380
gatgcagctg tttttaaccc acgttttat aggacctact tctttgtaga taaccagtat 1440
tggaggtatg atgaaaggag acagatgatg gaccctggtt atcccaaact gattaccaag 1500
aacttccaag gaatcgggcc taaaattgat gcagtcttct actctaaaaa caaatactac 1560
tatttcttcc aaggatctaa ccaatttgaa tatgacttcc tactccaacg tatcaccaaa 1620
acactgaaaa gcaatagctg gtttggttgt tag 1653

<210> 102
<211> 1416
<212> DNA
<213> Homo sapiens

<400> 102

atgcatccag gggtcctggc tgcctttcctc ttcttgagct ggactcattg tcgggccctg 60
cccctccca gtggtggtga tgaagatgat ttgtctgagg aagacctcca gtttgcagag 120
cgctacctga gatcatacta ccatcctaca aatctcgcgg gaatcctgaa ggagaatgca 180
gcaagctcca tgactgagag gctccgagaa atgcagtctt tcttcggctt agaggtgact 240
ggcaaacttg acgataacac cttagatgtc atgaaaaagc caagatgcgg ggttcctgat 300
gtgggtgaat acaatgtttt ccctcgaact cttaaatggt ccaaaatgaa tttaacctac 360
agaattgtga attacacccc tgatatgact cattctgaag tcgaaaaggc attcaaaaaa 420
gccttcaaag tttggtccga tgtaactcct cgaatttta ccagacttca cgatggcatt 480
gctgacatca tgatctcttt tggaattaag gagcatggcg acttctaccc atttgatggg 540
ccctctggcc tgctggctca tgcttttcct cctgggccaa attatggagg agatgcccat 600
tttgatgatg atgaaacctg gacaagtagt tccaaaggct acaacttgtt tcttgttgct 660
gcgcatgagt tcggccactc cttaggtctt gaccactcca aggaccctgg agcactcatg 720
tttcctatct acacctacac cggcaaaagc cactttatgc ttcctgatga cgatgtacaa 780
gggatccagt ctctctatgg tccaggagat gaagacccca accctaaaca tccaaaaacg 840
ccagacaaat gtgacccttc cttatccctt gatgccatta ccagtctccg aggagaaaca 900
atgatcttta aagacagatt cttctggcgc ctgcatcctc agcaggttga tgcggagctg 960
tttttaacga aatcattttg gccagaactt cccaaccgta ttgatgctgc atatgagcac 1020
ccttctcatg acctcatctt catcttcaga ggtagaaaat tttgggctct taatggttat 1080
gacattctgg aaggttatcc caaaaaaata tctgaactgg gtcttccaaa agaagttaag 1140
aagataagtg cagctgttca ctttgaggat acaggcaaga ctctcctgtt ctcaggaaac 1200
caggtctgga gatatgatga tactaaccat attatggata aagactatcc gagactaata 1260
gaagaagact tcccaggaat tggtgataaa gtagatgctg tctatgagaa aaatggttat 1320
atctattttt tcaacggacc catacagttt gaatacagca tctggagtaa ccgtattgtt 1380
cgcgtcatgc cagcaaattc cattttgtgg tgttaa 1416

<210> 103
<211> 1749
<212> DNA
<213> Homo sapiens

<300>
<302> MMP14
<310> NM004995

<400> 103
atgtctcccg ccccaagacc cccccgttgt ctcctgctcc ccctgctcac gctcggcacc 60
gcgctcgcct ccctcggctc ggcccaaagc agcagcttca gccccgaagc ctggctacag 120
caatatggct acctgcctcc cggggaccta cgtacccaca cacagcgctc accccagtca 180
ctctcagcgg ccatcgctgc catgcagaag ttttacggct tgcaagtaac aggcaaagct 240
gatgcagaca ccatgaaggc catgaggcgc ccccgatgtg gtgttccaga caagtttggg 300
gctgagatca aggccaatgt tcgaaggaag cgctacgcca tccagggtct caaatggcaa 360
catgatgaaa tcactttctg catccagaat tacaccccca aggtgggcga gtatgccaca 420
tacgaggcca ttcgcaaggc gttccgcgtg tgggagagtg ccacaccact gcgcttccgc 480
gaggtgccct atgcctacat ccgtgagggc catgagaagc aggccgacat catgatcttc 540
tttgccgagg gcttccatgg cgacagcacg cccttcgatg gtgagggcgg cttcctggcc 600
catgcctact tcccaggccc caacattgga ggagacaccc actttgactc tgccgagcct 660
tggactgtca ggaatgagga tctgaatgga aatgacatct tcctggtggc tgtgcacgag 720
ctgggccatg ccctgggggt cgagcattcc agtgacccct cggccatcat ggcaccctct 780
taccagtgga tggacacgga gaatttgtg ctgcccgatg atgaccgccg gggcatccag 840
caacttatg gggtgaggtc agggttcccc accaagatgc ccctccaacc caggactacc 900
tcccggcctt ctgttcctga taaacccaaa aaccccacct atgggcccaa catctgtgac 960
gggaacttg acaccgtggc catgctccga ggggagatgt ttgtcttcaa ggagcgctgg 1020
ttctggcggg tgaggaataa ccaagtgatg gatggatacc caatgcccat tggccagttc 1080
tggcggggcc tgcctgcgtc catcaacact gcctacgaga ggaaggatgt caaattcgtc 1140
ttcttcaaag gagacaagca ttgggtgttt gatgaggcgt ccctggaacc tggctacccc 1200
aagcacatta aggagctggg ccgagggctg cctaccgaca agattgatgc tgctctcttc 1260
tggatgccca atggaaagac ctacttcttc cgtggaaaca agtactaccg tttcaacgaa 1320
gagctcaggg cagtggatag cgagtacccc aagaacatca aagtctggga agggatccct 1380
gagtctccca gagggtcatt catgggcagc gatgaagtct tcacttactt ctacaagggg 1440

aacaaatact ggaaatttcaa caaccagaag ctgaaggtag aaccgggcta ccccaagtca 1500
gccctgaggg actggatggg ctgcccatcg ggaggccggc cggatgaggg gactgaggag 1560
gagacggagg tgatcatcat tgaggtggac gaggagggcg gcggggcggt gagcgcggct 1620
gccgtggtgc tgcccgtgct gctgctgctc ctggtgctgg cggtgggcct tgcagttctc 1680
ttcttcagac gccatgggac ccccaggcga ctgctctact gccagcgttc cctgctggac 1740
aaggtctga 1749

<210> 104
<211> 2010
<212> DNA
<213> Homo sapiens

<300>
<302> MMP15
<310> NM002428

<400> 104
atgggcagcg acccgagcgc gcccggacgg ccgggctgga cgggcagcct cctcggcgac 60
cgggaggagg cggcgcggcc gcgactgctg ccgctgctcc tggtgcttct gggctgcctg 120
ggccttggcg tagcggccga agacgcggag gtccatgccg agaactggct gcggctttat 180
ggctacctgc ctcagcccag ccgccatatg tccaccatgc gttccgccca gatcttggcc 240
tcggcccttg cagagatgca gcgctttctac gggatcccag tcaccggtgt gctcgacgaa 300
gagaccaagg agtggatgaa gcggccccgc tgtgggggtgc cagaccagtt cggggtacga 360
gtgaaagcca acctgcggcg gcgtcggaag cgctacgccc tcaccgggag gaagtggaac 420
aaccaccatc tgaccttag catccagaac tacacggaga agttgggctg gtaccactcg 480
atggaggcgg tgcgcagggc cttccgcgtg tgggagcagg ccacgccgct ggtcttccag 540
gaggtgccct atgaggacat ccggctgcgg cgacagaagg aggccgacat catggtactc 600
tttgcctctg gcttccacgg cgacagctcg ccgtttgatg gcaccggtgg ctttctggcc 660
cacgcctatt tccctggccc cggcctaggc ggggacaccc attttgacgc agatgagccc 720
tggaccttct ccagcactga cctgcatgga aacaacctct tcctggtggc agtgcatgag 780
ctgggccacg cgctggggct ggagcactcc agcaacccca atgccatcat ggcgccgttc 840
taccagtgga aggacgttga caacttcaag ctgcccgagg acgatctccg tggcatccag 900
cagctctacg gtaccccaga cggtcagcca cagcctaccc agcctctccc cactgtgacg 960
ccacggcggc caggccggcc tgaccaccgg ccgccccggc ctccccagcc accaccccca 1020
ggtgggaagc cagagcggcc cccaaagccg ggccccccag tccagcccca agccacagag 1080
cggcccgacc agtatggccc caacatctgc gacggggact ttgacacagt ggccatgctt 1140
cgcgggggaga tgttcgtgtt caagggccgc tggttctggc gagtccggca caaccgcgtc 1200
ctggacaact atcccatgcc catcgggcac ttctggcgtg gtctgcccgg tgacatcagt 1260
gctgcctacg agcgccaaga cggtcgtttt gtctttttca aaggtgaccg ctactggctc 1320
tttcgagaag cgaacctgga gcccggctac ccacagccgc tgaccagcta tggcctgggc 1380
atccctatg accgcattga cacggccatc tggtgggagc ccacaggcca caccttcttc 1440
ttccaagagg acaggtactg gcgcttcaac gaggagacac agcgtggaga ccctgggtac 1500
cccaagccca tcagtgtctg gcaggggatc cctgcctccc ctaaagggcc cttcctgagc 1560
aatgacgcag cctacaccta cttctacaag ggcaccaaat actggaaatt cgacaatgag 1620
cgcctgcgga tggagcccgg ctacccaag tccatcttgc gggacttcat gggctgccag 1680
gagcacgtgg agccaggccc ccgatggccc gacgtggccc ggccgccctt caaccccac 1740
gggggtgcag agcccggggc ggacagcgca gaggggacg tgggggatgg ggatggggac 1800
tttgggccg gggtcaacaa ggacgggggc agccgcgtgg tggtgcagat ggaggaggtg 1860
gcacggacgg tgaacgtggt gatggtgctg gtgccactgc tgctgctgct ctgcgtcctg 1920
ggcctcacct acgcgctggt gcagatgcag cgcaaggggtg cgccacgtgt cctgctttac 1980
tgcaagcgct cgctgcagga gtgggtctga 2010

<210> 105
<211> 1824
<212> DNA
<213> Homo sapiens

<300>

<302> MMP16
<310> NM005941

<400> 105
atgatcttac tcacattcag cactggaaga cggttggatt tcgtgcatca ttcgggggtg 60
ttttttcttgc aaaccttgct ttggatttta tgtgctacag tctgcggaac ggagcagtat 120
ttcaatgtgg aggtttggtt acaaaagtac ggctaccttc caccgactga ccccagaatg 180
tcagtgctgc gctctgcaga gaccatgcag tctgccctag ctgccatgca gcagttctat 240
ggcattaaca tgacaggaaa agtggacaga aacacaattg actggatgaa gaagccccga 300
tgcggtgtac ctgaccagac aagaggtagc tccaaatttc atattcgtcg aaagcgatat 360
gcattgacag gacagaaatg gcagcacaag cacatcactt acagtataaa gaacgtaact 420
ccaaaagtag gagaccctga gactcgtaaa gctattcgcc gtgcctttga tgtgtggcag 480
aatgtaactc ctctgacatt tgaagaagtt ccctacagtg aattagaaaa tggcaaacgt 540
gatgtggata taaccattat ttttgcatct ggtttccatg gggacagctc tccttttgat 600
ggagagggag gatttttggc acatgcctac ttccctggac caggaattgg aggagatacc 660
cattttgact cagatgagcc atggacacta ggaaatccta atcatgatgg aaatgactta 720
tttcttgtag cagtccatga actgggacat gctctgggat tggagcattc caatgacccc 780
actgccatca tggctccatt ttaccagtac atggaaacag acaacttcaa actacctaat 840
gatgatttac agggcatcca gaaaatatat ggtccacctg acaagattcc tccacctaca 900
agacctctac cgacagtgcc cccacaccgc tctattcctc cggctgaccc aaggaaaaat 960
gacaggccaa aacctcctcg gcctccaacc ggcagaccct cctatcccgg agccaaaccc 1020
aacatctgtg atgggaactt taacactcta gctattcttc gtcgtgagat gtttgttttc 1080
aaggaccagt ggttttggcg agtgagaaac aacagggtga tggatggata cccaatgcaa 1140
attacttact tctggcgggg cttgcctcct agtatcgatg cagtttatga aaatagcgac 1200
gggaattttg tgttctttaa aggtaacaaa tattgggtgt tcaaggatac aactcttcaa 1260
cctggttacc ctcatgactt gataaccctt ggaagtggaa ttccccctca tggtattgat 1320
tcagccattt ggtgggagga cgtcgggaaa acctatttct tcaagggaga cagatattgg 1380
agatatagtg aagaaatgaa aacaatggac cctggctatc ccaagccaat cacagtctgg 1440
aaagggatcc ctgaatctcc tcagggagca tttgtacaca aagaaaatgg ctttacgtat 1500
ttctacaaag gaaaggagta ttggaaattc aacaaccaga tactcaaggt agaacctgga 1560
catccaagat ccatcctcaa ggattttatg ggctgtgatg gaccaacaga cagagttaaa 1620
gaaggacaca gcccaccaga tgatgtagac attgtcatca aactggacaa cacgccagc 1680
actgtgaaag ccatagctat tgtcattccc tgcatcttgg ccttatgcct ccttgtattg 1740
gtttacactg tgttccagtt caagaggaaa ggaacacccc gccacatact gtactgtaaa 1800
cgctctatgc aagagtgggt gtga 1824

<210> 106
<211> 1560
<212> DNA
<213> Homo sapiens

<300>
<302> MMP17
<310> NM004141

<400> 106
atgcagcagt ttggtggcct ggaggccacc ggcatcctgg acgaggccac cctggccctg 60
atgaaaaccc cacgctgctc cctgccagac ctccctgtcc tgacccaggc tcgcaggaga 120
cgccaggctc cagcccccac caagtggaac aagaggaacc tgtcgtggag ggtccggacg 180
ttcccacggg actcaccact ggggcacgac acggtgcgtg cactcatgta ctacgccctc 240
aaggtctgga gcgacattgc gcccctgaac ttccacgagg tggcgggcag cacgccgac 300
atccagatcg acttctccaa ggccgaccat aacgacggct acccctttcga cggccccggc 360
ggcacccgtg cccacggctt cttccccggc caccaccaca ccgccggga cacccacttt 420
gacgatgacg aggcctggac cttccgctcc tcgggatgccc acgggatgga cctgtttgca 480
gtggctgtcc acgagtttgg ccacgccatt gggttaagcc atgtggccgc tgcacactcc 540
atcatgcggc cgtactacca gggcccggtg ggtgacccgc tgcgctacgg ggtcccctac 600
gaggacaagg tgcgcgtctg gcagctgtac ggtgtgcggg agtctgtgtc tcccacggcg 660
cagcccgagg agcctcccct gctgccggag cccccagaca accggtccag cgcccgccc 720
aggaaggacg tgccccacag atgcagcact cactttgacg cggtggccca gatccggggt 780

gaagctttct tcttcaaagg caagtacttc tggcggctga cgcgggaccg gcacctggtg 840
tccctgcagc cggcacagat gcaccgcttc tggcggggcc tgccgctgca cctggacagc 900
gtggacgccg tgtacgagcg caccagcgac cacaagatcg tcttctttaa aggagacagg 960
tactggggtgt tcaaggacaa taacgtagag gaaggatacc cgcgccccgt ctccgacttc 1020
agcctcccgc ctggcggcat cgacgctgcc ttctcctggg cccacaatga caggacttat 1080
ttctttaagg accagctgta ctggcgctac gatgaccaca cgaggcacat ggaccccggc 1140
taccccgccc agagcccact gtggaggggt gtccccagca cgctggacga cgccatgcgc 1200
tggtccgacg gtgcctccta cttcttccgt ggccaggagt actggaaagt gctggatggc 1260
gagctggagg tggcacccgg gtacccacag tccacggccc gggactggct ggtgtgtgga 1320
gactcacagg ccgatggatc tgtggctgcg ggcgtggacg cggcagaggg gccccgcgcc 1380
cctccaggac aacatgacca gagccgctcg gaggacggtt acgaggtctg ctcatgcacc 1440
tctggggcat cctctcccca gggggcccca ggcccactgg tggctgccac catgctgctg 1500
ctgctgccgc cactgtcacc aggcgccctg tggacagcgg cccaggccct gacgctatga 1560

<210> 107
<211> 1983
<212> DNA
<213> Homo sapiens

<300>
<302> MMP2
<310> NM004530

<400> 107
atggaggcgc taatggcccg gggcgcgctc acgggtcccc tgagggcgct ctgtctcctg 60
ggctgcctgc tgagccacgc cgccgccgcg ccgtcgccca tcatcaagtt ccccggcgat 120
gtcgccccca aaacggacaa agagttggca gtgcaatacc tgaacacctt ctatggctgc 180
cccaaggaga gctgcaacct gtttgtgctg aaggacacac taaagaagat gcagaagttc 240
tttggactgc cccagacagg tgatcttgac cagaatacca tcgagaccat gcggaagcca 300
cgctgcggca acccagatgt ggccaactac aacttcttcc ctcgcaagcc caagtgggac 360
aagaaccaga tcacatacag gatcattggc tacacacctg atctggaccc agagacagtg 420
gatgatgcct ttgctcgtgc cttccaagtc tggagcgatg tgaccccact gcggttttct 480
cgaatccatg atggagaggc agacatcatg atcaactttg gccgctggga gcatggcgat 540
ggatacccct ttgacggtaa ggacggactc ctggctcatg ccttcgcccc aggcactggt 600
gttgggggag actcccattt tgatgacgat gagctatgga ccttgggaga aggccaagtg 660
gtccgtgtga agtatggcaa cgccgatggg gagtactgca agttcccctt cttgttcaat 720
ggcaaggagt acaacagctg cactgatact ggccgcagcg atggcttcct ctggtgctcc 780
accacctaca actttgagaa ggatggcaag tacggcttct gtccccatga agccctgttc 840
accatgggcg gcaacgctga aggacagccc tgcaagtttc cattccgctt ccagggcaca 900
tcctatgaca gctgcaccac tgaggggccgc acggatggct accgctggtg cggcaccact 960
gaggactacg accgcgacaa gaagtatggc ttctgccctg agaccgccat gtccactgtt 1020
ggtgggaact cagaaggtgc cccctgtgtc ttccccttca ctttcctggg caacaaatat 1080
gagagctgca ccagccgccgg ccgcagtgac ggaaagatgt ggtgtgcgac cacagccaac 1140
tacgatgacg accgcaagtg gggcttctgc cctgaccaag ggtacagcct gttcctcgtg 1200
gcagcccacg agttttggcca cgccatgggg ctggagcact cccaagaccc tggggccctg 1260
atggcaccca ttacacctca caccaagaac ttccgtctgt cccaggatga catcaagggc 1320
attcaggagc tctatggggc ctctcctgac attgaccttg gcaccggccc caccccacaa 1380
ctgggccctg tcactcctga gatctgcaaa caggacattg tatttgatgg catcgctcag 1440
atccgtgggg agatcttctt cttcaaggac cggttcattt ggcggactgt gacgccacgt 1500
gacaagccca tgggccccct gctggtggcc acattctggc ctgagctccc ggaaaagatt 1560
gatgcggtat acgaggccca acaggaggag aaggctgtgt tctttgcagg gaatgaatac 1620
tggactctact cagccagcac cctggagcga gggtacccca agccactgac cagcctggga 1680
ctgcccctg atgtccagcg agtggatgcc gccttcaact ggagcaaaaa caagaagaca 1740
tacatctttg ctggagacaa attctggaga tacaatgagg tgaagaagaa aatggatcct 1800
ggcttcccca agctcatcgc agatgcctgg aatgccatcc ccgataacct ggatgccgtc 1860
gtggacctgc agggcggcgg tcacagctac ttcttcaagg gtgcctatta cctgaagctg 1920
gagaaccaaa gtctgaagag cgtgaagttt ggaagcatca aatccgactg gctaggctgc 1980
tga 1983

<210> 108
<211> 1434
<212> DNA
<213> Homo sapiens

<300>
<302> MMP2
<310> XM006271

<300>
<302> MMP3
<310> XM006271

<400> 108
atgaagagtc ttccaatcct actgttgctg tgcgtggcag tttgctcagc ctatccattg 60
gatggagctg caaggggtga ggacaccagc atgaaccttg ttcagaaata tctagaaaac 120
tactacgacc tcgaaaaaga tgtgaaacag tttgttagga gaaaggacag tggtcctgtt 180
gttaaaaaaa tccgagaaat gcagaagttc cttggattgg aggtgacggg gaagctggac 240
tccgacactc tggaggtgat gcgcaagccc aggtgtggag ttcctgacgt tggtcacttc 300
agaaccttc ctggcatccc gaagtggagg aaaacccacc ttacatacag gattgtgaat 360
tatacaccag atttgccaaa agatgctgtt gattctgctg ttgagaaagc tctgaaagtc 420
tgggaagagg tgactccact cacattctcc aggctgtatg aaggagaggc tgatatatg 480
atctcttttg cagttagaga acatggagac ttttaccctt ttgatggacc tggaaatgtt 540
ttggcccatg cctatgcccc tgggccaggg attaatggag atgcccactt tgatgatgat 600
gaacaatgga caaaggatac aacagggacc aatttatttc tcgttgctgc tcatgaaatt 660
ggccactccc tgggtctctt tcactcagcc aacactgaag ctttgatgta cccactctat 720
cactcactca cagacctgac tcggttccgc ctgtctcaag atgatataaa tggcattcag 780
tccctctatg gacctccccc tgactccct gagacccccc tggtacccac ggaacctgtc 840
cctccagaac ctgggacgcc agccaactgt gatcctgctt tgtcctttga tgctgtcagc 900
actctgaggg gagaaatcct gatctttaaa gacaggcact tttggcgcaa atccctcagg 960
aagcttgaac ctgaattgca tttgatctct tcattttggc catctcttcc ttcaggcgtg 1020
gatgccgcat atgaagttac tagcaaggac ctcgttttca tttttaaagg aaatcaattc 1080
tgggccatca gaggaaatga ggtacgagct ggatacccaa gaggcatcca caccctaggt 1140
ttccctccaa ccgtgaggaa aatcgatgca gccatttctg ataaggaaaa gaacaaaaca 1200
tatttctttg tagaggacaa atactggaga tttgatgaga agagaaattc catggagcca 1260
ggctttccca agcaaatagc tgaagacttt ccagggattg actcaaagat tgatgctgtt 1320
tttgaagaat ttgggttctt ttatttcttt actggatctt cacagttgga gtttgaccca 1380
aatgcaaaga aagtgacaca cactttgaag agtaacagct ggcttaattg ttga 1434

<210> 109
<211> 1404
<212> DNA
<213> Homo sapiens

<300>
<302> MMP8
<310> NM002424

<400> 109
atgttctccc tgaagacgct tccatttctg ctcttactcc atgtgcagat ttccaaggcc 60
tttcctgtat cttctaaaga gaaaaataca aaaactgttc aggactacct ggaaaagttc 120
taccaattac caagcaacca gtatcagtct acaaggaaga atggcactaa tgtgatcgtt 180
gaaaagctta aagaaatgca gcgatttttt gggttgaatg tgacgggggaa gccaaatgag 240
gaaactctgg acatgatgaa aaagcctcgc tgtggagtgc ctgacagtgg tggttttatg 300
ttaaccccag gaaaccccaa gtggggaacgc actaacttga cctacaggat tcgaaactat 360
accccacagc tgtcagaggc tgaggtagaa agagctatca aggatgcctt tgaactctgg 420
agtgttgcat cacctctcat cttcaccagg atctcacagg gagaggcaga tatcaacatt 480
gctttttacc aaagagatca cggtgacaat tctccatttg atggacccaa tggaatcctt 540

gctcatgcct ttcagccagg ccaaggtatt ggaggagatg ctcattttga tgccgaagaa 600
acatggacca acacctccgc aaattacaac ttgtttcttg ttgctgctca tgaatttggc 660
cattctttgg ggctcgctca ctcctctgac cctggtgcct tgatgtatcc caactatgct 720
ttcagggaaa ccagcaacta ctcactccct caagatgaca tcgatggcat tcaggccatc 780
tatggacttt caagcaaccc tatccaacct actggaccaa gcacacccaa accctgtgac 840
cccagtttga catttgatgc tatcaccaca ctccgtggag aaatactttt ctttaaagac 900
aggtacttct ggagaaggca tcctcagcta caaagagtcg aaatgaattt tatttctcta 960
ttctggccat cccttccaac tggtatacag gctgcttatg aagattttga cagagacctc 1020
attttcctat ttaaaggcaa ccaatactgg gctctgagtg gctatgatat tctgcaaggt 1080
tatcccaagg atatatcaaa ctatggcttc cccagcagcg tccaagcaat tgagcgcagt 1140
gtttttctaca gaagtaaaac atacttcttt gtaaatgacc aattctggag atatgataac 1200
caaagacaat tcatggagcc aggttatccc aaaagcatat caggtgcctt tccaggaata 1260
gagagtaaag ttgatgcagt tttccagcaa gaacatttct tccatgtctt cagtggacca 1320
agatattacg catttgatct tattgctcag agagttacca gagttgcaag aggcaataaa 1380
tggcttaact gtagatatgg ctga 1404

<210> 110
<211> 2124
<212> DNA
<213> Homo sapiens

<300>
<302> MMP9
<310> XM009491

<400> 110
atgagcctct ggcagcccct ggtcctggtg ctcctggtgc tgggctgctg ctttgctgcc 60
cccagacagc gccagtccac ccttgtgctc ttccctggag acctgagaac caatctcacc 120
gacaggcagc tggcagagga atacctgtac cgctatggtt acactcgggt ggcagagatg 180
cgtggagagt cgaaatctct ggggcctgcg ctgctgcttc tccagaagca actgtccctg 240
cccgagaccg gtgagctgga tagcgccacg ctgaaggcca tgcgaacccc acggtgcggg 300
gtcccagacc tgggcagatt ccaaaccttt gagggcgacc tcaagtggca ccaccacaac 360
atcacctatt ggatccaaaa ctactcggaa gacttgccgc gggcggtgat tgacgacgcc 420
tttgcccgcg ccttcgcact gtggagcgcg gtgacgccgc tcaccttcac tcgcgtgtac 480
agccgggacg cagacatcgt catccagttt ggtgtcgcgg agcacggaga cgggtatccc 540
ttcgacggga aggacgggct cctggcacac gcctttcctc ctggccccgg cattcaggga 600
gacgcccatt tcgacgatga cgagttgtgg tccctgggca agggcgtcgt ggttccaact 660
cggtttggaa acgcagatgg cgcggcctgc cacttcccct tcatcttcga gggccgctcc 720
tactctgcct gcaccaccga cggtcgctcc gacggcttgc cctggtgcag taccacggcc 780
aactacgaca ccgacgaccg gtttggcttc tgccccagcg agagactcta cacccaggac 840
ggcaatgctg atgggaaacc ctgccagttt ccattcatct tcacaaggcca atcctactcc 900
gcctgcacca cggacggtcg ctccgacggc taccgctggt gcgccaccac cgccaactac 960
gaccgggaca agctcttcgg cttctgcccg acccgagctg actcgacggt gatggggggc 1020
aactcggcgg gggagctgtg cgtcttcccc ttcactttcc tgggtaagga gtactcgacc 1080
tgtaccagcg agggccgcgg agatgggcgc ctctggtgcg ctaccacctc gaactttgac 1140
agcgacaaga agtggggctt ctgcccggac caaggataca gtttgttcct cgtggcggcg 1200
catgagttcg gccacgcgct gggcttagat cattcctcag tgccggaggc gctcatgtac 1260
cctatgtacc gcttcactga ggggcccccc ttgcataagg acgacgtgaa tggcatccgg 1320
cacctctatg gtcctcgccc tgaacctgag ccacggcctc caaccaccac cacaccgcag 1380
cccacggctc ccccgacggt ctgccccacc ggaccccccа ctgtccaccc ctcagagcgc 1440
cccacagctg gccccacagg tccccctca gctggcccca caggtccccc cactgctggc 1500
ccttctacgg ccactactgt gcctttgagt ccggtggacg atgcctgcaa cgtgaacatc 1560
ttcgacgcca tcgcggagat tgggaaccag ctgtatttgt tcaaggatgg gaagtactgg 1620
cgattctctg agggcagggg gagccggccg cagggccect tcctatcgc cgacaagtgg 1680
cccgcgtgc cccgcaagct ggactcggtc tttgaggagc ggctctccaa gaagcttttc 1740
ttcttcctg ggcgccaggt gtgggtgtac acaggcgcgt cggtgctggg cccgaggcgt 1800
ctggacaagc tggcctggg agccgacgtg gcccaggtga ccgggggccct ccggagtggc 1860
aggggaaga tgctgctgtt cagcgggcgg cgcctctgga ggttcgacgt gaaggcgcag 1920
atggtggatc cccggagcgc cagcgaggtg gaccggatgt tccccggggt gcctttggac 1980

```
acgcacgacg tcttccagta ccgagagaaa gcctatttct gccaggaccg cttctactgg 2040
cgcgtgagtt cccggagtga gttgaaccag gtggaccaag tgggctacgt gacctatgac 2100
atcctgcagt gccctgagga ctag                                        2124
```

<210> 111
<211> 2019
<212> DNA
<213> Homo sapiens

<300>
<302> PKC alpha
<310> NM002737

<400> 111
```
atggctgacg ttttcccggg caacgactcc acggcgtctc aggacgtggc caaccgcttc 60
gcccgcaaag gggcgctgag gcagaagaac gtgcacgagg tgaaggacca caaattcatc 120
gcgcgctttct tcaagcagcc caccttctgc agccactgca ccgacttcat ctgggggttt 180
gggaaacaag gcttccagtg ccaagtttgc tgttttgtgg tccacaagag gtgccatgaa 240
tttgttactt tttcttgtcc gggtgcggat aagggacccg acactgatga ccccaggagc 300
aagcacaagt tcaaaatcca cacttacgga agccccacct tctgcgatca ctgtgggtca 360
ctgctctatg gacttatcca tcaagggatg aaatgtgaca cctgcgatat gaacgttcac 420
aagcaatgcg tcatcaatgt ccccagcctc tgcggaatgg atcacactga gaagaggggg 480
cggatttacc taaaggctga ggttgctgat gaaaagctcc atgtcacagt acgagatgca 540
aaaaatctaa tccctatgga tccaaacggg ctttcagatc cttatgtgaa gctgaaactt 600
attcctgatc ccaagaatga aagcaagcaa aaaaccaaaa ccatccgctc cacactaaat 660
ccgcagtgga atgagtcctt tacattcaaa ttgaaacctt cagacaaaga ccgacgactg 720
tctgtagaaa tctgggactg ggatcgaaca acaaggaatg acttcatggg atcccttcc 780
tttggagttt cggagctgat gaagatgccg gccagtggat ggtacaagtt gcttaaccaa 840
gaagaaggtg agtactacaa cgtacccatt ccggaagggg acgaggaagg aaacatggaa 900
ctcaggcaga aattcgagaa agccaaactt ggccctgctg gcaacaaagt catcagtccc 960
tctgaagaca ggaaacaacc ttccaacaac cttgaccgag tgaaactcac ggacttcaat 1020
ttcctcatgg tgttgggaaa ggggagtttt ggaaaggtga tgcttgccga caggaagggc 1080
acagaagaac tgtatgcaat caaaatcctg aagaaggatg tggtgattca ggatgatgac 1140
gtggagtgca ccatggtaga aaagcgagtc ttggccctgc ttgacaaacc cccgttcttg 1200
acgcagctgc actcctgctt ccagacagtg gatcggctgt acttcgtcat ggaatatgtc 1260
aacggtgggg acctcatgta ccacattcag caagtaggaa aatttaagga accacaagca 1320
gtattctatg cggcagagat ttccatcgga ttgttctttc ttcataaaag aggaatcatt 1380
tatagggatc tgaagttaga taacgtcatg ttggattcag aaggacatat caaaattgct 1440
gactttggga tgtgcaagga acacatgatg gatggagtca cgaccaggac cttctgtggg 1500
actccagatt atatcgcccc agagataatc gcttatccagc cgtatggaaa atctgtggac 1560
tggtgggcct atggcgtcct gttgtatgaa atgcttgccg ggcagcctcc atttgatggt 1620
gaagatgaag acgagctatt tcagttctatc atggagcaca acgtttccta tccaaaatcc 1680
ttgtccaagg aggctgtttc tatctgcaaa ggactgatga ccaaacaccc agccaagcgg 1740
ctgggctgtg ggcctgaggg ggagagggac gtgagagagc atgccttctt ccggaggatc 1800
gactgggaaa aactggagaa cagggagatc cagccaccat tcaagcccaa agtgtgtggc 1860
aaaggagcag agaactttga caagttcttc acacgaggac agcccgtctt aacaccacct 1920
gatcagctgg ttattgctaa catagaccag tctgattttg aagggttctc gtatgtcaac 1980
ccccagtttg tgcacccccat cttacagagt gcagtatga                       2019
```

<210> 112
<211> 2022
<212> DNA
<213> Homo sapiens

<300>
<302> PKC beta
<310> X07109

<400> 112
atggctgacc cggctgcggg gccgccgccg agcgagggcg aggagagcac cgtgcgcttc 60
gcccgcaaag gcgccctccg gcagaagaac gtgcatgagg tcaagaacca caaattcacc 120
gcccgcttct tcaagcagcc caccttctgc agccactgca ccgacttcat ctggggcttc 180
gggaagcagg gattccagtg ccaagtttgc tgctttgtgg tgcacaagcg gtgccatgaa 240
tttgtcacat tctcctgccc tggcgctgac aagggtccag cctccgatga cccccgcagc 300
aaacacaagt ttaagatcca cacgtactcc agcccccacgt tttgtgacca ctgtgggtca 360
ctgctgtatg gactcatcca ccaggggatg aaatgtgaca cctgcatgat gaatgtgcac 420
aagcgctgcg tgatgaatgt tcccagcctg tgtggcacgg accacacgga gcgccgcggc 480
cgcatctaca tccaggccca catcgacagg gacgtcctca ttgtcctcgt aagagatgct 540
aaaaaccttg tacctatgga ccccaatggc ctgtcagatc cctacgtaaa actgaaactg 600
atccccgatc ccaaaagtga gagcaaacag aagaccaaaa ccatcaaatg ctccctcaac 660
cctgagtgga atgagacatt tagatttcag ctgaaagaat cggacaaaga cagaagactg 720
tcagtagaga tttgggattg ggatttgacc agcaggaatg acttcatggg atctttgtcc 780
tttgggattt ctgaacttca gaaggccagt gttgatggct ggtttaagtt actgagccag 840
gaggaaggcg agtacttcaa tgtgcctgtg ccaccagaag gaagtgaggc caatgaagaa 900
ctgcggcaga aatttgagag ggccaagatc agtcagggaa ccaaggtccc ggaagaaaag 960
acgaccaaca ctgtctccaa atttgacaac aatggcaaca gagaccggat gaaactgacc 1020
gattttaact tcctaatggt gctggggaaa ggcagctttg gcaaggtcat gctttcagaa 1080
cgaaaaggca cagatgagct ctatgctgtg aagaggacgt tgtgatccaa 1140
gatgatgacg tggagtgcac tatggtggag aagcgggtgt tggccctgcc tgggaagccg 1200
cccttcctga cccagctcca ctcctgcttc cagaccatgg accgcctgta ctttgtgatg 1260
gagtacgtga atggggggcga cctcatgtat cacatccagc aagtcggccg gttcaaggag 1320
ccccatgctg tattttacgc tgcagaaatt gccatcggtt tgttcttctt acagagtaag 1380
ggcatcattt accgtgacct aaaacttgac aacgtgatgc tcgattctga gggacacatc 1440
aagattgccg attttggcat gtgtaaggaa aacatctggg atggggtgac aaccaagaca 1500
ttctgtggca ctccagacta catcgccccc gagatgaattg cttatcagcc ctatgggaag 1560
tccgtggatt ggtgggcatt tggagtcctg ctgtatgaaa tgttggctgg gcaggcaccc 1620
tttgaagggg aggatgaaga tgaactcttc caatccatca tggaacacaa cgtagcctat 1680
cccaagtcta tgtccaagga agctgtggcc atctgcaaag ggctgatgac caaacaccca 1740
ggcaaacgtc tgggttgtgg acctgaaggc gaacgtgata tcaaagagca tgcatttttc 1800
cggtatattg attgggagaa acttgaacgc aaagagatcc agccccctta taagccaaaa 1860
gcttgtgggc gaaatgctga aaacttcgac cgatttttca cccgccatcc accagtccta 1920
acacctcccg accaggaagt catcaggaat attgaccaat cagaattcga aggattttcc 1980
tttgttaact ctgaattttt aaaacccgaa gtcaagagct aa 2022

<210> 113
<211> 2031
<212> DNA
<213> Homo sapiens

<300>
<302> PKC delta
<310> NM006254

<400> 113
atggcgccgt tcctgcgcat cgccttcaac tcctatgagc tgggctccct gcaggccgag 60
gacgaggcga accagccctt ctgtgccgtg aagatgaagg aggcgctcag cacagagcgt 120
gggaaaacac tggtgcagaa gaagccgacc atgtatcctg agtggaagtc gacgttcgat 180
gcccacatct atgaggggcg cgtcatccag attgtgctaa tgcgggcagc agaggagcca 240
gtgtctgagg tgaccgtggg tgtgtcggtg ctggccgagc gctgcaagaa gaacaatggc 300
aaggctgagt tctggctgga cctgcagcct caggccaagg tgttgatgtc tgttcagtat 360
ttcctggagg acgtggattg caaacaatct atggcgcagtg aggacgaggc caagtcccca 420
acgatgaacc gccgcggagc catcaaacag gccaaaatcc actacatcaa gaaccatgag 480
ttcatcgcca ccttctttgg gcaacccacc ttctgttctg tgtgcaaaga ctttgtctgg 540
ggcctcaaca agcaaggcta caaatgcagg caatgtaacg ctgccatcca caagaaatgc 600
atcgacaaga tcatcggcag atgcactggc accgcggcca acagccggga cactatattc 660
cagaaagaac gcttcaacat cgacatgccg caccgcttca aggttcacaa ctacatgagc 720
cccacctct gtgaccactg cggcagcctg ctctggggac tggtgaagca gggattaaag 780

tgtgaagact gcggcatgaa tgtgcaccat aaatgccggg agaaggtggc caacctctgc 840
ggcatcaacc agaagctttt ggctgaggcc ttgaaccaag tcacccagag agcctcccgg 900
agatcagact cagcctcctc agagcctgtt gggatatatc agggtttcga gaagaagacc 960
ggagttgctg gggaggacat gcaagacaac agtgggacct acggcaagat ctgggagggc 1020
agcagcaagt gcaacatcaa caacttcatc ttccacaagg tcctgggcaa aggcagcttc 1080
gggaaggtgc tgcttggaga gctgaagggc agaggagagt actctgccat caagtcccta 1140
aagaaggatg tggtcctgat cgacgacgac gtggagtgca ccatggttga gaagcgggtg 1200
ctgacacttg ccgcagagaa tccctttctc acccacctca tctgcacctt ccagaccaag 1260
gaccacctgt tctttgtgat ggagttcctc aacgggggag acctgatgta ccacatccag 1320
gacaaaggcc gctttgaact ctaccgtgcc acgttttatg ccgctgagat aatgtgtgga 1380
ctgcagtttc tacacagcaa gggcatcatt tacagggacc tcaaactgga caatgtgctg 1440
ttggaccggg atggccacat caagattgcc gactttggga tgtgcaaaga gaacatattc 1500
ggggagagcc gggccagcac cttctgcggc accccтgact atatcgcccc tgagatccta 1560
cagggcctga agtacacatt ctctgtggac tggtggtctt tcggggtcct tctgtacgag 1620
atgctcattg gccagtcccc cttccatggt gatgatgagg atgaactctt cgagtccatc 1680
cgtgtggaca cgccacatta tccccgctgg atcaccaagg agtccgagga tatcctggag 1740
aagctctttg aaagggaacc aaccaagagg ctgggaatga cgggaaacat caaaatccac 1800
ccctttctca agaccataaa ctggactctg ctggaaaagc ggaggttgga gcaccccttc 1860
aggcccaaag tgaagtcacc cagagactac agtaactttg accaggagtt cctgaacgag 1920
aaggcgcgcc tctcctacag cgacaagaac ctcatcgact ccatggacca gtctgcattc 1980
gctggcttct cctttgtgaa ccccaaattc gagcacctcc tggaagattg a 2031

<210> 114
<211> 2049
<212> DNA
<213> Homo sapiens

<300>
<302> PKC eta
<310> NM006255

<400> 114
atgtcgtctg gcaccatgaa gttcaatggc tatttgaggg tccgcatcgg tgaggcagtg 60
gggctgcagc ccacccgctg gtccctgcgc cactcgctct tcaagaaggg ccaccagctg 120
ctggacccct atctgacggt gagcgtggac caggtgcgcg tgggccagac cagcaccaag 180
cagaagacca acaaacccac gtacaacgag gagttttgcg ctaacgtcac cgacggcggc 240
cacctcgagt tggccgtctt ccacgagacc cccctgggct acgacttcgt ggccaactgc 300
accctgcagt tccaggagct cgtcggcacg accggcgcct cgagcacctt cgaggttgg 360
gtggatctcg agccagaggg gaaagtattt gtggtaataa cccttaccgg gagtttcact 420
gaagctactc tccagagaga ccggatcttc aaacatttta ccaggaagcg ccaaaggcct 480
atgcgaaggc gagtccacca gatcaatgga cacaagttca tggccacgta tctgaggcag 540
cccacctact gctctcactg cagggagttt atctgggggag tgtttgggaa acaggttat 600
cagtgccaag tgtgcacctg tgtcgtccat aaacgctgcc atcatctaat tgttacagcc 660
tgtacttgcc aaaacaatat taacaaagtg gattcaaaga ttgcagaaca gaggttcggg 720
atcaacatcc cacacaagtt cagcatccac aactacaaag tgccaacatt ctgcgatcac 780
tgtggctcac tgctctgggg aataatgcga caaggacttc agtgtaaaat atgtaaaatg 840
aatgtgcata ttcgatgtca agcgaacgtg gcccctaact gtggggtaaa tgcggtggaa 900
cttgccaaga ccctggcagg gatgggtctc caacccggaa atatttctcc aacctcgaaa 960
ctcgtttcca gatcgaccct aagacgacag ggaaaggaga gcagcaaaga aggaaatggg 1020
attgggggtta attcttccaa ccgacttggt atcgacaact ttgagttcat ccgagtgttg 1080
gggaagggga gttttgggaa ggtgatgctt gcaagagtaa aagaaacagg agacctctat 1140
gctgtgaagg tgctgaagaa ggacgtgatt ctgctggatg atgatgtgga atgcaccatg 1200
accgagaaaa ggatcctgtc tctggccgc aatcacccct tcctcactca gttgttctgc 1260
tgctttcaga ccccgatcg tctgtttttt gtgatggagt tggtgaatgg gggtgacttg 1320
atgttccaca ttcagaagtc tcgtcgtttt gatgaagcac gagctcgctt ctatgctgca 1380
gaaatcattt cggctctcat gttcctccat gataaaggaa tcatctatag agatctgaaa 1440
ctggacaatg tcctgttgga ccacgagggt cactgtaaac tggcagactt cggaatgtgc 1500
aaggagggga tttgcaatgg tgtcaccacg gccacattct gtggcacgcc agactatatc 1560
gctccagaga tcctccagga aatgctgtac gggcctgcag tagactggtg ggcaatgggc 1620

gtgttgctct atgagatgct ctgtggtcac gcgccttttg aggcagagaa tgaagatgac 1680
ctctttgagg ccatactgaa tgatgaggtg gtctacccta cctggctcca tgaagatgcc 1740
acagggatcc taaaatcttt catgaccaag aaccccacca tgcgcttggg cagcctgact 1800
cagggaggcg agcacgccat cttgagacat ccttttttta aggaaatcga ctgggcccag 1860
ctgaaccatc gccaaataga accgcctttc agacccagaa tcaaatcccg agaagatgtc 1920
agtaattttg accctgactt cataaaggaa gagccagttt taactccaat tgatgaggga 1980
catcttccaa tgattaacca ggatgagttt agaaactttt cctatgtgtc tccagaattg 2040
caaccatag 2049

<210> 115
<211> 948
<212> DNA
<213> Homo sapiens

<300>
<302> PKC epsilon
<310> XM002370

<400> 115
atgttggcag aactcaaggg caaagatgaa gtatatgctg tgaaggtctt aaagaaggac 60
gtcatccttc aggatgatga cgtggactgc acaatgacag agaagaggat tttggctctg 120
gcacggaaac acccgtacct tacccaactc tactgctgct tccagaccaa ggaccgcctc 180
tttttcgtca tggaatatgt aaatggtgga gacctcatgt ttcagattca gcgctcccga 240
aaattcgacg agcctcgttc acggttctat gctgcagagg tcacatcggc cctcatgttc 300
ctccaccagc atggagtcat ctacagggat ttgaaactgg acaacatcct tctggatgca 360
gaaggtcact gcaagctggc tgacttcggg atgtgcaagg aagggattct gaatggtgtg 420
acgaccacca cgttctgtgg gactcctgac tacatagctc ctgagatcct gcaggagttg 480
gagtatggcc cctccgtgga ctggtgggcc ctgggggtgc tgatgtacga gatgatggct 540
ggacagcctc cctttgaggc cgacaatgag gacgacctat ttgagtccat cctccatgac 600
gacgtgctgt acccagtctg gctcagcaag gaggctgtca gcatcttgaa agctttcatg 660
acgaagaatc cccacaagcg cctgggctgt gtggcatcgc agaatggcga ggacgccatc 720
aagcagcacc cattcttcaa agagattgac tgggtgctcc tggagcagaa gaagatcaag 780
ccacccttca aaccacgcat taaaaccaaa agagacgtca atatattttga ccaagacttt 840
acccgggaag agccggtact cacccttgtg gacgaagcaa ttgtaaagca gatcaaccag 900
gaggaattca aaggtttctc ctactttggt gaagacctga tgccctga 948

<210> 116
<211> 1764
<212> DNA
<213> Homo sapiens

<300>
<302> PKC iota
<310> NM002740

<400> 116
atgtcccaca cggtcgcagg cggcggcagc ggggaccatt cccaccaggt ccgggtgaaa 60
gcctactacc gcggggatat catgataaca catttgaac cttccatctc ctttgagggc 120
ctttgcaatg aggttcgaga catgtgttct tttgacaacg aacagctctt caccatgaaa 180
tggatagatg aggaaggaga cccgtgtaca gtatcatctc agttggagtt agaagaagcc 240
tttagacttt atgagctaaa caaggattct gaactcttga ttcatgtgtt cccttgtgta 300
ccagaacgtc ctgggatgcc ttgtccagga gaagataaat ccatctaccg tagaggtgca 360
cgccgctgga gaaagcttta ttgtgccaat ggccacactt tccaagccaa gcgtttcaac 420
aggcgtgctc actgtgccat ctgcacagac cgaatatggg gacttggacg ccaaggatat 480
aagtgcatca actgcaaact cttggttcat aagaagtgcc ataaactcgt cacaattgaa 540
tgtgggcggc attctttgcc acaggaacca gtgatgccca tggatcagtc atccatgcat 600
tctgaccatg cacagacagt aattccatat aatccttcaa gtcatgagag ttttgatcaa 660
gttggtgaag aaaaagaggc aatgaacacc agggaaagtg gcaaagcttc atccagtcta 720

ggtcttcagg attttgattt gctccgggta ataggaagag gaagttatgc caaagtactg 780
ttggttcgat taaaaaaaac agatcgtatt tatgcaatga aagttgtgaa aaaagagctt 840
gttaatgatg atgaggatat tgattgggta cagacagaga agcatgtgtt tgagcaggca 900
tccaatcatc ctttccttgt tgggctgcat tcttgctttc agacagaaag cagattgttc 960
tttgttatag agtatgtaaa tggaggagac ctaatgtttc atatgcagcg acaaagaaaa 1020
cttcctgaag aacatgccag attttactct gcagaaatca gtctagcatt aaattatctt 1080
catgagcgag ggataattta tagagatttg aaactggaca atgtattact ggactctgaa 1140
ggccacatta aactcactga ctacggcatg tgtaaggaag gattacggcc aggagataca 1200
accagcactt tctgtggtac tcctaattac attgctcctg aaatttttaag aggagaagat 1260
tatggttcta gtgttgactg gtgggctctt ggagtgctca tgtttgagat gatggcagga 1320
aggtctccat ttgatattgt tgggagctcc gataaccctg accagaacac agaggattat 1380
ctctttccaag ttattttgga aaaacaaatt cgcataccac gttctctgtc tgtaaaagct 1440
gcaagtgttc tgaagagttt tcttaataag gaccctaagg aacgattggg ttgtcatcct 1500
caaacaggat ttgctgatat tcagggacac ccgttcttcc gaaatgttga ttgggatatg 1560
atggagcaaa aacaggtggt acctccctttt aaaccaaata tttctgggga atttggtttg 1620
gacaactttg attctcagtt tactaatgaa cctgtccagc tcactccaga tgacgatgac 1680
attgtgagga agattgatca gtctgaattt gaaggttttg agtatatcaa tcctcttttg 1740
atgtctgcag aagaatgtgt ctga 1764

<210> 117
<211> 2451
<212> DNA
<213> Homo sapiens

<300>
<302> PKC mu
<310> XM007234

<400> 117
atgtatgata agatcctgct ttttcgccat gaccctacct ctgaaaacat ccttcagctg 60
gtgaaagcgg ccagtgatat ccaggaaggc gatcttattg aagtggtctt gtcagcttcc 120
gccacctttg aagactttca gattcgtccc cacgctctct ttgttcattc atacagagct 180
ccagctttct gtgatcactg tggagaaatg ctgtgggggc tggtacgtca aggtctttaaa 240
tgtgaagggt gtggtctgaa ttaccataag agatgtgcat ttaaaatacc caacaattgc 300
agcggtgtga ggcggagaag gctctcaaac gtttccctca ctggggtcag caccatccgc 360
acatcatctg ctgaactctc tacaagtgcc cctgatgagc cccttctgca aaaatcacca 420
tcagagtcgt ttattggtcg agagaagagg tcaaattctc aatcatacat tggacgacca 480
attcaccttg acaagatttt gatgtctaaa gttaaagtgc cgcacacatt tgtcatccac 540
tcctacaccc ggcccacagt gtgccagtac tgcaagaagc ttctgaaggg gcttttcagg 600
cagggcttgc agtgcaaaga ttgcagattc aactgccata aacgttgtgc accgaaagta 660
ccaaacaact gccttggcga agtgaccatt aatggagatt tgcttagccc tggggcagag 720
tctgatgtgg tcatggaaga agggagtgat gacaatgata gtgaaaggaa cagtgggctc 780
atggatgata tggaagaagc aatggtccaa gatgcagaga tggcaatggc agagtgccag 840
aacgacagtg gcgagatgca agatccagac ccagaccacg aggacgccaa cagaaccatc 900
agtccatcaa caagcaacaa tatcccactc atgagggtag tgcagtctgt caaacacacg 960
aagaggaaaa gcagcacagt catgaaagaa ggatggatgg tccactacac cagcaaggac 1020
acgctgcgga aacggcacta ttggagattg gatagcaaat gtattaccct ctttcagaat 1080
gacacaggaa gcaggtacta caaggaaatt cctttatctg aaatttttgtc tctggaacca 1140
gtaaaaactt cagctttaat tcctaatggg gccaatcctc attgtttcga aatcactacg 1200
gcaaatgtag tgtattatgt gggagaaaat gtggtcaatc ctccagccc atcaccaaat 1260
aacagtgttc tcaccagtgg cgttggtgca gatgtggcca ggatgtggga gatagccatc 1320
cagcatgccc ttatgcccgt cattcccaag ggctcctccg tgggtacagg aaccaacttg 1380
cacagagata tctctgtgag tatttcagta tcaaattgcc agattcaaga aaatgtggac 1440
atcagcacag tatatcagat ttttcctgat gaagtactgg gttctggaca gtttggaatt 1500
gtttatggag gaaaacatcg taaaacagga agagatgtag ctattaaaat cattgacaaa 1560
ttacgatttc caacaaaaca agaaagccag cttcgtaatg aggttgcaat tctacagaac 1620
cttcatcacc ctggtgttgt aaatttggag tgtatgtttg agacgcctga aagagtgttt 1680
gttgttatgg aaaaactcca tggagacatg ctggaaatga tcttgtcaag tgaaaagggc 1740
aggttgccag agcacataac gaagttttta attactcaga tactcgtggc tttgcggcac 1800

cttcatttta aaaatatcgt tcactgtgac ctcaaaccag aaaatgtgtt gctagcctca 1860
gctgatcctt ttcctcaggt gaaactttgt gattttggtt ttgcccggat cattggagag 1920
aagtctttcc ggaggtcagt ggtgggtacc cccgcttacc tggctcctga ggtcctaagg 1980
aacaagggct acaatcgctc tctagacatg tggtctgttg gggtcatcat ctatgtaagc 2040
ctaagcggca cattcccatt taatgaagat gaagacatac acgaccaaat tcagaatgca 2100
gctttcatgt atccaccaaa tccctggaag gaaatatctc atgaagccat tgatcttatc 2160
aacaatttgc tgcaagtaaa aatgagaaag cgctacagtg tggataagac cttgagccac 2220
ccttggctac aggactatca gacctggtta gatttgcgag agctggaatg caaaatcggg 2280
gagcgctaca tcacccatga aagtgatgac ctgaggtggg agaagtatgc aggcgagcag 2340
gggctgcagt accccacaca cctgatcaat ccaagtgcta gccacagtga cactcctgag 2400
actgaagaaa cagaaatgaa agccctcggt gagcgtgtca gcatcctatg a 2451

<210> 118
<211> 2673
<212> DNA
<213> Homo sapiens

<300>
<302> PKC nu
<310> NM005813

<400> 118
atgtctgcaa ataattcccc tccatcagcc cagaagtctg tattacccac agctattcct 60
gctgtgcttc cagctgcttc tccgtgttca agtcctaaga cgggactctc tgcccgactc 120
tctaatggaa gcttcagtgc accatcactc accaactcca gaggctcagt gcatacagtt 180
tcatttctac tgcaaattgg cctcacacgg gagagtgtta ccattgaagc ccaggaactg 240
tctttatctg ctgtcaagga tcttgtgtgc tccatagttt atcaaaagtt tccagagtgt 300
ggattctttg gcatgtatga caaaattctt ctctttcgcc atgacatgaa ctcagaaaac 360
attttgcagc tgattacctc agcagatgaa atactgaag gagacctagt ggaagtggtt 420
ctttcagctt tagccacagt agaagacttc cagattcgtc cacatacttc ctatgtacat 480
tcttacaaag ctcctacttt ctgtgattac tgtggtgaga tgctgtgggg attggtacgt 540
caaggactga aatgtgaagg ctgtggatta aattaccata aacgatgtgc cttcaagatt 600
ccaaataact gtagtggagt aagaaagaga cgtctgtcaa atgtatcttt accaggaccc 660
ggcctctcag ttccaagacc cctacagcct gaatatgtag cccttcccag tgaagagtca 720
catgtccacc aggaaccaag taagagaatt ccttcttgga gtggtcgccc aatctggatg 780
gaaaagatgg taatgtgcag agtgaaagtt ccacacacat tcttgcttca ctcttacacc 840
cgtcccacga tatgtcagta ctgcaagcgg ttactgaaag gcctctttcg ccaaggaatg 900
cagtgtaaag attgcaaatt caactgccat aaacgctgtg catcaaaagt accaagagac 960
tgccttggag aggttacttt caatggagaa ccttccagtc tgggaacaga tacagatata 1020
ccaatggata ttgacaataa tgacataaat agtgatagta gtcgggggttt ggatgacaca 1080
gaagagccat caccccaga agataagatg ttcttcttgg atccatctga tctcgatgtg 1140
gaaagagatg aagaagccgt taaaacaatc agtccatcaa caagcaataa tattccgcta 1200
atgaggggtg tacaatccat caagcacaca aagaggaaga gcagcacaat ggtgaaggaa 1260
gggtggatgg tccattacac cagcagggat aacctgagaa agaggcatta ttggagactt 1320
gacagcaaat gtctaacatt atttcagaat gaatctggat caaagtatta taaggaaatt 1380
ccacttcag aaattctccg catatcttca ccacgagatt tcacaaacat ttcacaaggc 1440
agcaatccac actgttttga aatcattact gatactatgg tatacttcgt tggtgagaac 1500
aatgggaca gctctcataa tcctgttctt gctgccactg gagttggact tgatgtagca 1560
cagagctggg aaaaagcaat tcgccaagcc ctcatgcctg ttactcctca agcaagtgtt 1620
tgcacttctc cagggcaagg gaaagatcac aaagatttgt ctacaagtat ctctgtatct 1680
aattgtcaga ttcaggagaa tgtggatatc agtactgttt accagatctt tgcagatgag 1740
gtgcttggtt caggccagtt tggcatcgtt tatggaggaa aacatagaaa gactggagag 1800
gatgtggcta ttaaagtaat tgataagatg agattcccca caaaacaaga aagtcaactc 1860
cgtaatgaag tggctatttt acagaatttg caccatcctg ggattgtaaa cctggaatgt 1920
atgtttgaaa ccccagaacg agtctttgta gtaatggaaa agctgcatgg agatatgttg 1980
gaaatgattc tatccagtga gaaaagtcgg cttccagaac gaattactaa attcatggtc 2040
acacagatac ttgttgcttt gaggaatctg cattttaaga atattgtgca ctgtgattta 2100
aagccagaaa atgtgctgct tgcatcagca gagccatttc ctcaggtgaa gctgtgtgac 2160
tttggatttg cacgcatcat tggtgaaaag tcattcagga gatctgtggt aggaactcca 2220

gcatacttag cccctgaagt tctccggagc aaaggttaca accgttccct agatatgtgg 2280
tcagtgggag ttatcatcta tgtgagcctc agtggcacat ttccttttaa tgaggatgaa 2340
gatataaatg accaaatcca aaatgctgca tttatgtacc caccaaatcc atggagagaa 2400
atttctggtg aagcaattga tctgataaac aatctgcttc aagtgaagat gagaaaacgt 2460
tacagtgttg acaaatctct tagtcatccc tggctacagg actatcagac ttggcttgac 2520
cttagagaat ttgaaactcg cattggagaa cgttacatta cacatgaaag tgatgatgct 2580
cgctgggaaa tacatgcata cacacataac cttgtatacc caaagcactt cattatggct 2640
cctaatccag atgatatgga agaagatcct taa 2673

<210> 119
<211> 2121
<212> DNA
<213> Homo sapiens

<300>
<302> PKC tau
<310> NM006257

<400> 119
atgtcgccat ttcttcggat tggcttgtcc aactttgact gcgggtcctg ccagtcttgt 60
cagggcgagg ctgttaaccc ttactgtgct gtgctcgtca aagagtatgt cgaatcagag 120
aacgggcaga tgtatatcca gaaaaagcct accatgtacc caccctggga cagcactttt 180
gatgcccata tcaacaaggg aagagtcatg cagatcattg tgaaaggcaa aaacgtggac 240
ctcatctctg aaaccaccgt ggagctctac tcgctggctg agaggtgcag gaagaacaac 300
gggaagacag aaatatggtt agagctgaaa cctcaagggc gaatgctaat gaatgcaaga 360
tactttctgg aaatgagtga cacaaaggac atgaatgaat ttgagacgga aggcttcttt 420
gctttgcatc agcgccgggg tgccatcaag caggcaaagg tccaccacgt caagtgccac 480
gagttcactg ccacctttct cccacagccc acattttgct ctgtctgcca cgagtttgtc 540
tggggcctga acaaacaggg ctaccagtgc cgacaatgca atgcagcaat tcacaagaag 600
tgtattgata aagttatagc aaagtgcaca ggatcagcta tcaatagccg agaaaccatg 660
ttccacaagg agagattcaa aattgacatg ccacacagat ttaaagtcta caattacaag 720
agcccgacct tctgtgaaca ctgtgtgggc ctgctgtggg gactggcacg gcaaggactc 780
aagtgtgatg catgtggcat gaatgtgcat catagatgcc agacaaaggt ggccaacctt 840
tgtggcataa accagaagct aatggctgaa gcgctggcca tgattgagag cactcaacag 900
gctcgctgct taagagatac tgaacagatc ttcagagaag gtccggttga aattggtctc 960
ccatgctcca tcaaaaatga agcaaggccg ccatgtttac cgacaccggg aaaaagagag 1020
cctcagggca tttcctggga gtctccgttg gatgaggtgg ataaaatgtg ccatcttcca 1080
gaacctgaac tgaacaaaga aagaccatct ctgcagatta aactaaaaat tgaggatttt 1140
atcttgcaca aaatgttggg gaaaggaagt tttggcaagg tcttcctggc agaattcaag 1200
aaaaccatcc aattttcgc aataaaggcc ttaaagaaag atgtggtctt gatggacgat 1260
gatgttgagt gcacgatggt agagaagaga gttctttcct tggcctggga gcatccgttt 1320
ctgacgcaca tgttttgtac attccagacc aaggaaaacc tcttttttgt gatggagtac 1380
ctcaacggag gggacttaat gtaccacatc caaagctgcc acaagttcga cctttccaga 1440
gcgacgttt atgctgctga aatcattctt ggtctgcagt tccttcattc caaaggaata 1500
gtctacaggg acctgaagct agataacatc ctgttagaca aagatggaca tatcaagatc 1560
gcggatttg gaatgtgcaa ggagaacatg ttaggagatg ccaagacgaa taccttctgt 1620
gggacacctg actacatcgc ccccagagatc ttgctgggtc agaaatacaa ccacttctgt 1680
gactggtggt ccttcggggt tctccttat gaaatgctga ttggtcagtc gcctttccac 1740
gggcaggatg aggaggagct cttccactcc atccgcatgg acaatccctt ttacccacgg 1800
tggctggaga aggaagcaaa ggaccttctg gtgaagctct tcgtgcgaga acctgagaag 1860
aggctgggcg tgaggggaga catccgccag caccctttgt ttcgggagat caactgggag 1920
gaacttgaac ggaaggagat tgacccaccg ttccggccga aagtgaaatc accatttgac 1980
tgcagcaatt tcgacaaaga attcttaaac gagaagcccc ggctgtcatt tgccgacaga 2040
gcactgatca acagcatgga ccagaatatg ttcaggaact tttccttcat gaaccccggg 2100
atggagcggc tgatatcctg a 2121

<210> 120
<211> 1779

<212> DNA
<213> Homo sapiens

<300>
<302> PKC zeta
<310> NM2744

<400> 120
atgcccagca ggaccgaccc caagatggaa gggagcggcg gccgcgtccg cctcaaggcg 60
cattacgggg gggacatctt catcaccagc gtggacgccg ccacgacctt cgaggagctc 120
tgtgaggaag tgagagacat gtgtcgtctg caccagcagc acccgctcac cctcaagtgg 180
gtggacagcg aaggtgaccc ttgcacggtg tcctcccaga tggagctgga agaggctttc 240
cgcctggccc gtcagtgcag ggatgaaggc ctcatcattc atgttttccc gagcacccct 300
gagcagcctg gcctgccatg tccgggagaa gacaaatcta tctaccgccg gggagccaga 360
agatggagga agctgtaccg tgccaacggc cacctcttcc aagccaagcg ctttaacagg 420
agagcgtact gcggtcagtg cagcgagagg atatggggcc tcgcgaggca aggctacagg 480
tgcatcaact gcaaactgct ggtccataag cgctgccacg gcctcgtccc gctgacctgc 540
aggaagcata tggattctgt catgccttcc caagagcctc cagtagacga caagaacgag 600
gacgccgacc ttccttccga ggagacagat ggaattgctt acatttcctc atcccggaag 660
catgacagca ttaaagacga ctcggaggac cttaagccag ttatcgatgg gatggatgga 720
atcaaaatct ctcaggggct tgggctgcag gactttgacc taatcagagt catcgggcgc 780
gggagctacg ccaaggttct cctggtgcgg ttgaagaaga atgaccaaat ttacgccatg 840
aaagtggtga agaaagagct ggtgcatgat gacgaggata ttgactgggt acagacagag 900
aagcacgtgt ttgagcaggc atccagcaac cccttcctgg tcggattaca ctcctgcttc 960
cagacgacaa gtcggttgtt cctggtcatt gagtacgtca acggcgggga cctgatgttc 1020
cacatgcaga ggcagaggaa gctccctgag gagcacgcca ggttctacgc ggccgagatc 1080
tgcatcgccc tcaacttcct gcacgagagg gggatcatct acagggacct gaagctggac 1140
aacgtcctcc tggatgcgga cgggcacatc aagctcacag actacggcat gtgcaaggaa 1200
ggcctgggcc ctggtgacac aacgagcact ttctgcggaa ccccgaatta catcgccccc 1260
gaaatcctgc ggggagagga gtacgggttc agcgtggact ggtgggcgct gggagtcctc 1320
atgtttgaga tgatggccgg gcgctccccg ttcgacatca tcaccgacaa cccggacatg 1380
aacacagagg actacctttt ccaagtgatc ctggagaagc ccatccggat ccccccggtt 1440
ctgtccgtca aagcctccca tgttttaaaa ggatttttaa ataaggaccc caaagagagg 1500
ctcggctgcc ggccacagac tggattttct gacatcaagt cccacgcgtt cttccgcagc 1560
atagactggg acttgctgga gaagaagcag gcgctccctc catttccagcc acagatcaca 1620
gacgactacg gtctggacaa ctttgacaca cagttcacca gcgagcccgt gcagctgacc 1680
ccagacgatg aggatgccat aaagaggatc gaccagtcag agttcgaagg ctttgagtat 1740
atcaacccat tattgctgtc caccgaggag tcggtgtga 1779

<210> 121
<211> 576
<212> DNA
<213> Homo sapiens

<300>
<302> VEGF
<310> NM003376

<400> 121
atgaactttc tgctgtcttg ggtgcattgg agccttgcct tgctgctcta cctccaccat 60
gccaagtggt cccaggctgc acccatggca gaaggaggag ggcagaatca tcacgaagtg 120
gtgaagttca tggatgtcta tcagcgcagc tactgccatc caatcgagac cctggtggac 180
atcttccagg agtacgctga tgagatcgag tacatcttca agccatcctg tgtgccccgg 240
atgcgatgcg gggctgctg caatgacgag ggcctggagt gtgtgcccac tgaggagtcc 300
aacatcacca tgcagattat gcggatcaaa cctcaccaag gccagcacat aggagagatg 360
agcttcctac agcacaacaa atgtgaatgc agaccaaaga agatagagc aagacaagaa 420
aatccctgtg ggccttgctc agagcggaga aagcatttgt ttgtacaaga tccgcagacg 480
tgtaaatgtt cctgcaaaaa cacagactcg cgttgcaagg cgaggcagct tgagttaaac 540
gaacgtactt gcagatgtga caagccgagg cggtga 576

<210> 122
<211> 624
<212> DNA
<213> Homo sapiens

<300>
<302> VEGF B
<310> NM003377

<400> 122
atgagccctc tgctccgccg cctgctgctc gccgcactcc tgcagctggc ccccgcccag 60
gcccctgtct cccagcctga tgcccctggc caccagagga aagtggtgtc atggatagat 120
gtgtatactc gcgctacctg ccagccccgg gaggtggtgg tgcccttgac tgtggagctc 180
atgggcaccg tggccaaaca gctggtgccc agctgcgtga ctgtgcagcg ctgtggtggc 240
tgctgccctg acgatggcct ggagtgtgtg cccactgggc agcaccaagt ccggatgcag 300
atcctcatga tccggtaccc gagcagtcag ctgggggaga tgtccctgga agaacacagc 360
cagtgtgaat gcagacctaa aaaaaaggac agtgctgtga agccagacag ggctgccact 420
ccccaccacc gtccccagcc ccgttctgtt ccgggctggg actctgcccc cggagcaccc 480
tccccagctg acatcaccca tcccactcca gccccaggcc cctctgccca cgctgcaccc 540
agcaccacca gcgccctgac ccccggacct gccgccgccg ctgccgacgc cgcagcttcc 600
tccgttgcca agggcggggc ttag 624

<210> 123
<211> 1260
<212> DNA
<213> Homo sapiens

<300>
<302> VEGF C
<310> NM005429

<400> 123
atgcacttgc tgggcttctt ctctgtggcg tgttctctgc tcgccgctgc gctgctcccg 60
ggtcctcgcg aggcgcccgc cgccgccgcc gccttcgagt ccggactcga cctctcggac 120
gcggagcccg acgcgggcga ggccacggct tatgcaagca aagatctgga ggagcagtta 180
cggtctgtgt ccagtgtaga tgaactcatg actgtacttc acccagaata ttggaaaatg 240
tacaagtgtc agctaaggaa aggaggctgg caacatataa gagaacaggc caaccttcaac 300
tcaaggacag aagagactat aaaatttgct gcagcacatt ataatacaga gatcttgaaa 360
agtattgata atgagtggag aaagactcaa tgcatgccac gggaggtgtg tatagatgtg 420
gggaaggagt ttggagtcgc gacaaacacc ttctttaaac ctccatgtgt gtccgtctac 480
agatgtgggg gttgctgcaa tagtgagggg ctgcagtgca tgaacaccag cacgagctac 540
ctcagcaaga cgttatttga aattacagtg cctctctctc aaggccccaa accagtaaca 600
atcagtttg ccaatcacac ttcctgccga tgcatgtcta aactggatgt ttacagacaa 660
gttcattcca ttattagacg ttccctgcca gcaacactac cacagtgtca ggcagcgaac 720
aagacctgcc ccaccaatta catgtggaat aatcacatct gcagatgcct ggctcaggaa 780
gattttatgt tttcctcgga tgctggagat gactcaacag atggattcca tgacatcttgt 840
ggaccaaaca aggagctgga tgaagagacc tgtcagtgtg tctgcagagc ggggcttcgg 900
cctgccagct gtggacccca caaagaacta gacagaaact catgccagtg tgtctgtaaa 960
aacaaactct tccccagcca atgtggggcc aaccgagaat ttgatgaaaa cacatgccag 1020
tgtgtatgta aaagaacctg ccccagaaat caacccctaa atcctggaaa atgtgcctgt 1080
gaatgtacag aaagtccaca gaaatgcttg ttaaaaggaa agaagttcca ccaccaaaca 1140
tgcagctgtt acagacggcc atgtacgaac cgccagaagg cttgtgagcc aggattttca 1200
tatagtgaag aagtgtgtcg ttgtgtccct tcatattgga aaagaccaca aatgagctaa 1260

<210> 124
<211> 1074

<212> DNA
<213> Homo sapiens

<300>
<302> VEGF D
<310> AJ000185

<400> 124
atattcaaaa tgtacagaga gtgggtagtg gtgaatgttt tcatgatgtt gtacgtccag 60
ctggtgcagg gctccagtaa tgaacatgga ccagtgaagc gatcatctca gtccacattg 120
gaacgatctg aacagcagat cagggctgct tctagtttgg aggaactact tcgaattact 180
cactctgagg actggaagct gtggagatgc aggctgaggc tcaaaagttt taccagtatg 240
gactctcgct cagcatccca tcggtccact aggtttgcgg caactttcta tgacattgaa 300
acactaaaag ttatagatga agaatggcaa agaactcagt gcagccctag agaaacgtgc 360
gtggaggtgg ccagtgagct ggggaagagt accaacacat tcttcaagcc cccttgtgtg 420
aacgtgttcc gatgtggtgg ctgttgcaat gaagagagcc ttatctgtat gaacaccagc 480
acctcgtaca tttccaaaca gctctttgag atatcagtgc ctttgacatc agtacctgaa 540
ttagtgcctg ttaaagttgc caatcataca ggttgtaagt gcttgccaac agccccccgc 600
catccatact caattatcag aagatccatc cagatccctg aagaagatcg ctgttcccat 660
tccaagaaac tctgtcctat tgacatgcta tgggatagca acaaatgtaa atgtgttttg 720
caggaggaaa atccacttgc tggaacagaa gaccactctc atctccagga accagctctc 780
tgtgggccac acatgatgtt tgacgaagat cgttgcgagt gtgtctgtaa aacaccatgt 840
cccaaagatc taatccagca ccccaaaaac tgcagttgct ttgagtgcaa agaaagtctg 900
gagacctgct gccagaagca caagctattt cacccagaca cctgcagctg tgaggacaga 960
tgccccttc ataccagacc atgtgcaagt ggcaaaacag catgtgcaaa gcattgccgc 1020
tttccaaagg agaaaagggc tgcccagggg ccccacagcc gaaagaatcc ttga 1074

<210> 125
<211> 1314
<212> DNA
<213> Homo sapiens

<300>
<302> E2F
<310> M96577

<400> 125
atggccttgg ccggggcccc tgcgggcggc ccatgcgcgc cggcgctgga ggccctgctc 60
ggggccggcg cgctgcggct gctcgactcc tcgcagatcg tcatcatctc cgccgcgcag 120
gacgccagcg ccccgccggc tcccaccggc cccgcggcgc ccgccgccgg cccctgcgac 180
cctgacctgc tgctctttcgc cacaccgcag gcgccccggc ccacacccag tgcgccgcgg 240
cccgcgctcg gccgcccgcc ggtgaagcgg aggctggacc tggaaactga ccatcagtac 300
ctggccgaga gcagtgggcc agctcggggc agaggccgcc atccaggaaa aggtgtgaaa 360
tccccggggg agaagtcacg ctatgagacc tcactgaatc tgaccaccaa gcgcttcctg 420
gagctgctga gccactcggc tgacggtgtc gtcgacctga actggctgc cgaggtgctg 480
aaggtgcaga agcggcgcat ctatgacatc accaacgtcc ttgagggcat ccagctcatt 540
gccaagaagt ccaagaacca catccagtgg ctgggcagcc acaccacagt gggcgtcggc 600
ggacggcttg aggggttgac ccaggacctc cgacagctgc aggagagcga gcagcagctg 660
gaccacctga tgaatatctg tactacgcag ctgcgcctgc tctccgagga cactgacagc 720
cagcgcctgg cctacgtgac gtgtcaggac cttcgtagca ttgcagaccc tgcagagcag 780
atggttatgg tgatcaaagc ccctcctgag acccagctcc aagccgtgga ctcttcggag 840
aacttcaga tctccctaa gagcaaacaa ggcccgatcg atgttttcct gtgcctgag 900
gagaccgtag gtgggatcag ccctgggaag accccatccc aggaggtcac ttctgaggag 960
gagaacaggg ccactgactc tgccaccata gtgtcaccac caccatcatc tccccctca 1020
tccctcacca cagatcccag ccagtctcta ctcagcctgg agcaagaacc gctgttgtcc 1080
cggatgggca gcctgcgggc tccgtggtac gaggaccgcc tgtcccgcgt ggtggcggcc 1140
gactcgctcc tggagcatgt gcgggaggac ttctccggcc tcctccctga ggagttcatc 1200
agccttccc cacccacga ggccctcgac taccacttcg gcctcgagga gggcgagggc 1260
atcagagacc tcttcgactg tgactttggg gacctcaccc ccctggattt ctga 1314

<210> 126
<211> 166
<212> DNA
<213> Human papillomavirus

<300>
<302> EBER-1
<310> Jo2078

<400> 126
ggacctacgc tgccctagag gttttgctag ggaggagacg tgtgtggctg tagccacccg 60
tcccgggtac aagtcccggg tggtgaggac ggtgtctgtg gttgtcttcc cagactctgc 120
tttctgccgt cttcggtcaa gtaccagctg gtggtccgca tgtttt 166

<210> 127
<211> 172
<212> DNA
<213> Hepatitis C virus

<300>
<302> EBER-2
<310> J02078

<400> 127
ggacagccgt tgccctagtg gtttcggaca caccgccaac gctcagtgcg gtgctaccga 60
cccgaggtca agtcccgggg gaggagaaga gaggcttccc gcctagagca tttgcaagtc 120
aggattctct aatccctctg ggagaagggt attcggcttg tccgctattt tt 172

<210> 128
<211> 651
<212> DNA
<213> Hepatitis C virus

<300>
<302> NS2
<310> AJ238799

<400> 128
atggaccggg agatggcagc atcgtgcgga ggcgcggttt tcgtaggtct gatactcttg 60
accttgtcac cgcactataa gctgttcctc gctaggctca tatggtggtt acaatatttt 120
atcaccaggg ccgaggcaca cttgcaagtg tggatccccc ccctcaacgt tcgggggggc 180
cgcgatgccg tcatcctcct cacgtgcgcg atccacccag agctaatctt taccatcacc 240
aaaatcttgc tcgccatact cggtccactc atggtgctcc aggctggtat aaccaaagtg 300
ccgtacttcg tgcgccacca cgggctcatt cgtgcatgca tgctggtgcg gaaggttgct 360
gggggtcatt atgtccaaat ggctctcatg aagttggccg cactgacagg tacgtacgtt 420
tatgaccatc tcaccccact gcgggactgg gcccacgcgg gcctacgaga ccttgcggtg 480
gcagttgagc ccgtcgtctt ctctgatatg gagaccaagg ttatcacctg gggggcagac 540
accgcggcgt gtggggacat catcttgggc ctgcccgtct ccgcccgcag ggggagggag 600
atacatctgg gaccggcaga cagccttgaa gggcaggggt ggcgactcct c 651

<210> 129
<211> 161
<212> DNA
<213> Hepatitis C virus

<300>
<302> NS4A
<310> AJ238799

<400> 129
gcacctgggt gctggtaggc ggagtcctag cagctctggc cgcgtattgc ctgacaacag 60
gcagcgtggt cattgtgggc aggatcatct tgtccggaaa gccggccatc attcccgaca 120
gggaagtcct ttaccgggag ttcgatgaga tggaagagtg c 161

<210> 130
<211> 783
<212> DNA
<213> Hepatitis C virus

<300>
<302> NS4B
<310> AJ238799

<400> 130
gcctcacacc tcccttacat cgaacaggga atgcagctcg ccgaacaatt caaacagaag 60
gcaatcgggt tgctgcaaac agccaccaag caagcggagg ctgctgctcc cgtggtggaa 120
tccaagtggc ggaccctcga agccttctgg gcgaagcata tgtggaattt catcagcggg 180
atacaatatt tagcaggctt gtccactctg cctggcaacc ccgcgatagc atcatgatg 240
gcattcacag cctctatcac cagcccgctc accacccaac atacctcct gtttaacatc 300
ctgggggtgat gggtggccgc ccaacttgct cctcccagcg ctgcttctgc tttcgtaggc 360
gccggcatcg ctggagcggc tgttggcagc ataggccttg ggaaggtgct tgtggatatt 420
ttggcaggtt atggagcagg ggtggcaggc gcgctcgtgg cctttaaggt catgagcggc 480
gagatgccct ccaccgagga cctggttaac ctactccctg ctatcctctc ccctggcgcc 540
ctagtcgtcg gggtcgtgtg cgcagcgata ctgcgtcggc acgtgggccc aggggagggg 600
gctgtgcagt ggatgaaccg gctgatagcg ttcgctttcgc ggggtaacca cgtctccccc 660
acgcactatg tgcctgagag cgacgctgca gcacgtgtca ctcagatcct ctctagtctt 720
accatcactc agctgctgaa gaggcttcac cagtggatca acgaggactg ctccacgcca 780
tgc 783

<210> 131
<211> 1341
<212> DNA
<213> Hepatitis C virus

<300>
<302> NS5A
<310> AJ238799

<400> 131
tccggctcgt ggctaagaga tgtttgggat tggatatgca cggtgttgac tgatttcaag 60
acctggctcc agtccaagct cctgccgcga ttgccgggag tccccttctt ctcatgtcaa 120
cgtgggtaca agggagtctg gcggggcgac ggcatcatgc aaaccacctg cccatgtgga 180
gcacagatca ccggacatgt gaaaaacggt tccatgagga tcgtgggggcc taggacctgt 240
agtaacacgt ggcatggaac attcccctt aacgcgtaca ccacgggccc ctgcacgccc 300
tcccccggcgc caaattattc tagggcgctg tggcgggtgg ctgctgagga gtacgtggag 360
gttacgcggg tgggggattt ccactacgtg acgggcatga ccactgacaa cgtaaagtgc 420
ccgtgtcagg ttccggcccc cgaattcttc acagaagtgg atgggggtgcg gttgcacagg 480
tacgctccag cgtgcaaacc cctcctacgg gaggaggtca cattcctggt cgggctcaat 540
caataacttgg ttgggtcaca gctcccatgc gagcccgaac cggacgtagc agtgctcact 600
tccatgctca ccgacccctc ccacattacg gcggagacgg ctaagcgtag gctggccagg 660
ggatctcccc cctccttggc cagctcatca gctagccagc tgtctgcgcc ttccttgaag 720
gcaacatgca ctacccgtca tgactccccg gacgctgacc tcatcgaggc caacctcctg 780
tggcggcagg agatgggcgg gaacatcacc cgcgtggagt cagaaaataa ggtagtaatt 840

ttggactctt tcgagccgct ccaagcggag gaggatgaga gggaagtatc cgttccggcg 900
gagatcctgc ggaggtccag gaaattccct cgagcgatgc ccatatgggc acgccggat 960
tacaaccctc cactgttaga gtcctggaag gacccggact acgtccctcc agtggtacac 1020
gggtgtccat tgccgcctgc caaggcccct ccgataccac ctccacggag gaagaggacg 1080
gttgtcctgt cagaatctac cgtgtcttct gccttggcgg agctcgccac aaagaccttc 1140
ggcagctccg aatcgtcggc cgtcgacagc ggcacggcaa cggcctctcc tgaccagccc 1200
tccgacgacg gcgacgcggg atccgacgtt gagtcgtact cctccatgcc ccccctgag 1260
ggggagccgg gggatcccga tctcagcgac gggtcttggt ctaccgtaag cgaggaggct 1320
agtgaggacg tcgtctgctg c 1341

<210> 132
<211> 1772
<212> DNA
<213> Hepatitis C virus

<300>
<302> NS5B
<310> AJ238799

<400> 132
tcgatgtcct acacatggac aggcgccctg atcacgccat gcgctgcgga ggaaaccaag 60
ctgcccatca atgcactgag caactctttg ctccgtcacc acaacttggt ctatgctaca 120
acatcttcgca gcgcaagcct gcggcagaag aaggtcacct ttgacagact gcaggtcctg 180
gacgaccact accgggacgt gctcaaggag atgaaggcga aggcgtccac agttaaggct 240
aaacttctat ccgtggagga agcctgtaag ctgacgcccc cacattcggc cgactctaaa 300
tttggctatg gggcaaagga cgtccggaac ctatccagca aggccgttaa ccacatccgc 360
tccgtgtgga aggacttgct ggaagacact gagcaccaa ttgacaccac catcatggca 420
aaaaatgagg ttttctgcgt ccaaccagag aagggggggcc gcaagccagc tcgccttatc 480
gtattcccag atttgggggt tcgtgtgtgc gagaaaatgg ccctttacga tgtggtctcc 540
accctccctc aggccgtgat gggctcttca tacggattcc aatactctcc tggacagcgg 600
gtcgagttcc tggtgaatgc ctggaaagcg aagaaatgcc ctatgggctt cgcatatgac 660
acccgctgtt ttgactcaac ggtcactgag aatgacatcc gtgttgagga gtcaatctac 720
caatgttgtg acttggcccc cgaagccaga caggccataa ggtcgctcac agagcggctt 780
tacatcgggg gcccctgac taatttctaaa gggcagaact gcggctatcg ccggtgccgc 840
gcgagcggtg tactgacgac cagctgcggt aataccctca catgttactt gaaggccgct 900
gcggcctgtc gagctgcgaa gctccaggac tgcacgatgc tcgtatgcgg agacgacctt 960
gtcgttatct gtgaaagcgc ggggacccaa gaggacgagg cgagcctacg ggccttcacg 1020
gaggctatga ctagatactc tgccccccct ggggacccgc ccaaaccaga atacgacttg 1080
gagttgataa catcatgctc ctccaatgtg tcagtcgcgc acgatgcatc tggcaaaagg 1140
gtgtactatc tcacccgtga ccccacccacc ccccttgcgc gggctgcgtg ggagacagct 1200
agacacactc cagtcaattc ctggctaggc aacatcatca tgtatgcgcc caccttgtgg 1260
gcaaggatga tcctgatgac tcatttcttc tccatccttc tagctcagga acaacttgaa 1320
aaagccctag attgtcagat ctacggggcc tgttactcca ttgagccact tgacctacct 1380
cagatcattc aacgactcca tggccttagc gcatttttcac tccatagtta ctctccaggt 1440
gagatcaata gggtggcttc atgcctcagg aaacttgggg taccgccctt gcgagtctgg 1500
agacatcggg ccagaagtgt ccgcgctagg ctactgtccc agggggggag ggctgccact 1560
tgtggcaagt acctcttcaa ctgggcagta aggaccaagc tcaaactcac tccaatcccg 1620
gctgcgtccc agttggattt atccagctgg ttcgttgctg gttacagcgg gggagacata 1680
tatcacagcc tgtctcgtgc ccgaccccgc tggttcatgt ggtgcctact cctactttct 1740
gtaggggtag gcatctatct actccccaac cg 1772

<210> 133
<211> 1892
<212> DNA
<213> Hepatitis C virus

<300>
<302> NS3

<310> AJ238799

<400> 133
cgcctattac ggcctactcc caacagacgc gaggcctact tggctgcatc atcactagcc 60
tcacaggccg ggacaggaac caggtcgagg gggaggtcca agtggtctcc accgcaacac 120
aatctttcct ggcgacctgc gtcaatggcg tgtgttggac tgtctatcat ggtgccggct 180
caaagaccct tgccggccca aagggcccaa tcaccccaaat gtacaccaat gtggaccagg 240
acctcgtcgg ctggcaagcg ccccccgggg cgcgttcctt gacaccatgc acctgcggca 300
gctcggacct ttacttggtc acgaggcatg ccgatgtcat tccggtgcgc cggcggggcg 360
acagcagggg gagcctactc tcccccaggc ccgtctccta cttgaagggc tcttcgggcg 420
gtccactgct ctgcccctcg gggcacgctg tgggcatctt tcgggctgcc gtgtgcaccc 480
gaggggttgc gaaggcggtg gactttgtac ccgtcgagtc tatggaaacc actatgcggt 540
ccccggtctt cacggacaac tcgtccccctc cggccgtacc gcagacattc caggtggccc 600
atctacacgc ccctactggt agcggcaaga gcactaaggt gccggctgcg tatgcagccc 660
aagggtataa ggtgcttgtc ctgaacccgt ccgtcgccgc caccctaggt ttcggggcgt 720
atatgtctaa ggcacatggt atcgacccta acatcagaac cggggtaagg accatcacca 780
cgggtgcccc catcacgtac tccacctatg gcaagtttct tgccgacggt ggttgctctg 840
ggggcgccta tgacatcata atatgtgatg agtgccactc aactgactcg accactatcc 900
tgggcatcgg cacagtcctg gaccaagcgg agacggctgg agcgcgactc gtcgtgctcg 960
ccaccgctac gcctccggga tcggtcaccg tgccacatcc aaacatcgag gaggtggctc 1020
tgtccagcac tggagaaatc ccctttttatg gcaaagccat ccccatcgag accatcaagg 1080
gggggaggca cctcattttc tgccattcca agaagaaatg tgatgagctc gccgcgaagc 1140
tgtccggcct cggactcaat gctgtagcat attaccgggg ccttgatgta tccgtcatac 1200
caactagcgg agacgtcatt gtcgtagcaa cggacgctct aatgacgggc tttaccggcg 1260
atttcgactc agtgatcgac tgcaatacat gtgtcaccca gacagtcgac ttcagcctgg 1320
acccgacctt caccattgag acgacgaccg tgccacaaga cgcggtgtca cgctcgcagc 1380
ggcgaggcag gactggtagg ggcaggatgg gcatttacag gtttgtgact ccaggagaac 1440
ggccctcggg catgttcgat tcctcggttc tgtgcgagtg ctatgacgcg ggctgtgctt 1500
ggtacgagct cacgcccgcc gagacctcag ttaggttgcg ggcttaccta aacacaccag 1560
ggttgcccgt ctgccaggac catctggagt tctgggagag cgtcttaca ggcctcaccc 1620
acatagacgc ccatttcttg tcccagacta agcaggcagg agacaacttc ccctacctgg 1680
tagcatacca ggctacggtg tgcgccaggg ctcaggctcc acctccatcg tggaccaaaa 1740
tgtggaagtg tctcatacgg ctaaagccta cgctgcacgg gccaacgccc ctgctgtata 1800
ggctgggagc cgttcaaaac gaggttacta ccacacaccc cataaccaaa tacatcatgg 1860
catgcatgtc ggctgacctg gaggtcgtca cg 1892

<210> 134
<211> 822
<212> DNA
<213> Homo sapiens

<300>
<302> stmn cell factor
<310> M59964

<400> 134
atgaagaaga cacaaacttg gattctcact tgcatttatc ttcagctgct cctatttaat 60
cctctcgtca aaactgaagg gatctgcagg aatcgtgtga ctaataatgt aaaagacgtc 120
actaaattgg tggcaaatct tccaaaagac tacatgataa ccctcaaata tgtccccggg 180
atggatgttt tgccaagtca ttgttggata agcgagatgg tagtacaatt gtcagacagc 240
ttgactgatc ttctggacaa gttttcaaat atttctgaag gcttgagtaa ttattccatc 300
atagacaaac ttgtgaatat agtcgatgac cttgtggagt gcgtcaaaga aaactcatct 360
aaggatctaa aaaaatcatt caagagccca gaacccaggc tctttactcc tgaagaattc 420
tttagaattt ttaatagatc cattgatgcc ttcaaggact ttgtagtggc atctgaaact 480
agtgattgtg tggtttcttc aacattaagt cctgagaaag attccagagt cagtgtcaca 540
aaaccattta tgttaccccc tgttgcagcc agctcccttа ggaatgacag cagtagcagt 600
aataggaagg ccaaaaatcc ccctggagac tccagcctac actgggcagc catggcattg 660
ccagcattgt tttctcttat aattggcttt gcttttggag ccttatactg gaagaagaga 720
cagccaagtc ttacaagggc agttgaaaat atacaaatta atgaagagga taatgagata 780

agtatgttgc aagagaaaga gagagagttt caagaagtgt aa 822

<210> 135
<211> 483
<212> DNA
<213> Homo sapiens

<300>
<302> TGFalpha
<310> AF123238

<400> 135
atggtcccct cggctggaca gctcgccctg ttcgctctgg gtattgtgtt ggctgcgtgc 60
caggccttgg agaacagcac gtccccgctg agtgcagacc cgccgtggc tgcagcagtg 120
gtgtcccatt ttaatgactg cccagattcc cacactcagt tctgcttcca tggaacctgc 180
aggtttttgg tgcaggagga caagccagca tgtgtctgcc atttcgggta cgttggtgca 240
cgctgtgagc atgcggacct cctggccgtg gtggctgcca gccagaagaa gcaggccatc 300
accgccttgg tggtggtctc catcgtggcc ctggctgtcc ttatcatcac atgtgtgctg 360
atacactgct gccaggtccg aaaacactgt gagtggtgcc gggccctcat ctgccggcac 420
gagaagccca gcgccctcct gaagggaaga accgcttgct gccactcaga aacagtggtc 480
tga 483

<210> 136
<211> 1071
<212> DNA
<213> Homo sapiens

<300>
<302> GD3 synthase
<310> NM003034

<400> 136
atgagcccct gcgggcgggc ccggcgacaa acgtccagag gggccatggc tgtactggcg 60
tggaagttcc cgcggacccg gctgcccatg ggagccagtg ccctctgtgt cgtggtcctc 120
tgttggctct acatctttccc cgtctaccgg ctgcccaacg agaaagagat cgtgcagggg 180
gtgctgcaac agggcacggc gtggaggagg aaccagaccg cggccagagc gttcaggaaa 240
caaatggaag actgctgcga ccctgcccat ctctttgcta tgactaaaat gaattccccct 300
atgggaaga gcatgtggta tgacggggag tttttatact cattcaccat tgacaattca 360
acttactctc tcttcccaca ggcaacccca ttccagctgc cattgaagaa atgcgcggtg 420
gtgggaaatg gtgggattct gaagaagagt ggctgtggcc gtcaaataga tgaagcaaat 480
tttgtcatgc gatgcaatct ccctcctttg tcaagtgaat acactaagga tgttggatcc 540
aaaagtcagt tagtgacagc taatcccagc ataattcggc aaaggtttca gaaccttctg 600
tggtccagaa agacatttgt ggacaacatg aaaatctata accacagtta catctacatg 660
cctgcctttt ctatgaagac aggaacagag ccatctttga gggtttatta tacactgtca 720
gatgttggtg ccaatcaaac agtgctgttt gccaacccca actttctgcg tagcattgga 780
aagttctgga aaagtagagg aatccatgcc aagcgcctgt ccacaggact ttttctggtg 840
agctgagctc tgggtctctg tgaagaggtg gccatctatg gcttctggcc cttctctgtg 900
aatatgcatg agcagcccat cagccaccac tactatgaca acgtcttacc cttttctggc 960
ttccatgcca tgcccgagga atttctccaa ctctggtatc ttcataaaat cggtgcactg 1020
agaatgcagc tggacccatg tgaagatacc tcactccagc ccacttccta g 1071

<210> 137
<211> 744
<212> DNA
<213> Homo sapiens

<300>

<302> FGF14
<310> NM004115

<400> 137
atggccgcgg ccatcgctag cggcttgatc cgccagaagc ggcaggcgcg ggagcagcac 60
tgggaccggc cgtctgccag caggaggcgg agcagcccca gcaagaaccg cgggctctgc 120
aacggcaacc tggtggatat cttctccaaa gtgcgcatct tcggcctcaa gaagcgcagg 180
ttgcggcgcc aagatcccca gctcaagggt atagtgacca ggttatattg caggcaaggc 240
tactacttgc aaatgcaccc cgatggagct ctcgatggaa ccaaggatga cagcactaat 300
tctacactct tcaacctcat accagtggga ctacgtgttg ttgccatcca gggagtgaaa 360
acagggttgt atatagccat gaatggagaa ggttacctct acccatcaga actttttacc 420
cctgaatgca agtttaaaga atctgttttt gaaaattatt atgtaatcta ctcatccatg 480
ttgtacagac aacaggaatc tggtagagcc tggtttttgg gattaaataa ggaagggcaa 540
gctatgaaag ggaacagagt aaagaaaacc aaaccagcag ctcatttttct acccaagcca 600
ttggaagttg ccatgtaccg agaaccatct ttgcatgatg ttggggaaac ggtcccgaag 660
cctgggggtga cgccaagtaa aagcacaagt gcgttctgcaa taatgaatgg aggcaaacca 720
gtcaacaaga gtaagacaac atag 744

<210> 138
<211> 1503
<212> DNA
<213> Human immunodeficiency virus

<300>
<302> gag (HIV)
<310> NC001802

<400> 138
atgggtgcga gagcgtcagt attaagcggg ggagaattag atcgatggga aaaaattcgg 60
ttaaggccag ggggaaagaa aaaatataaa ttaaaacata tagtatgggc aagcagggag 120
ctagaacgat tcgcagttaa tcctggcctg ttagaaacat cagaaggctg tagacaaata 180
ctgggacagc tacaaccatc ccttcagaca ggatcagaag aacttagatc attatataat 240
acagtagcaa ccctctattg tgtgcatcaa aggatagaga taaaagacac caaggaagct 300
ttagacaaga tagaggaaga gcaaaacaaa agtaagaaaa aagcacagca agcagcagct 360
gacacaggac acagcaatca ggtcagccaa aattacccta tagtgcagaa catccagggg 420
caaatggtac atcaggccat atcacctaga actttaaatg catgggtaaa agtagtagaa 480
gagaaggctt tcagcccaga agtgataccc atgttttcag cattatcaga aggagccacc 540
ccacaagatt taaacaccat gctaaacaca gtggggggac atcaagcagc catgcaaatg 600
ttaaaagaga ccatcaatga ggaagctgca gaatgggata gagtgcatcc agtgcatgca 660
gggcctattg caccaggcca gatgagagaa ccaaggggaa gtgacatagc aggaactact 720
agtacccttc aggaacaaat aggatggatg acaaataatc cacctatccc agtaggagaa 780
atttataaaa gatggataat cctgggatta aataaaatag taagaatgta tagccctacc 840
agcattctgg acataagaca aggaccaaag gaacccttta gagactatgt agaccggttc 900
tataaaactc taagagccga gcaagcttca caggaggtaa aaaattggat gacagaaacc 960
ttgttggtcc aaaatgcgaa cccagattgt aagactattt taaaagcatt gggaccagcg 1020
gctacactag aagaaatgat gacagcatgt cagggagtag gaggacccgg ccataaggca 1080
agagtttttg ctgaagcaat gagccaagta acaaattcag ctaccataat gatgcagaga 1140
ggcaatttta ggaaccaaag aaagattgtt aagtgtttca attgtggcaa agaagggcac 1200
acagccagaa attgcagggc ccctaggaaa aagggctgtt ggaaatgtgg aaaggaagga 1260
caccaaatga aagattgtac tgagagacag gctaatttttt tagggaagat ctggccttcc 1320
tacaagggaa ggccagggaa ttttcttcag agcagaccag agccaacagc cccaccagaa 1380
gagagcttca ggtctggggt agagacaaca actccccctc agaagcagga gccgatagac 1440
aaggaactgt atcctttaac ttccctcagg tcactctttg gcaacgaccc ctcgtcacaa 1500
taa 1503

<210> 139
<211> 1101
<212> DNA

<213> Human immunodeficiency virus

<300>
<302> TARBP2
<310> NM004178

<400> 139
atgagtgaag aggagcaagg ctccggcact accacgggct gcgggctgcc tagtatagag 60
caaatgctgg ccgccaaccc aggcaagacc ccgatcagcc ttctgcagga gtatgggacc 120
agaatagggа agacgcctgt gtacgacctt ctcaaagccg agggccaagc ccaccagcct 180
aatttcacct tccgggtcac cgttggcgac accagctgca ctggtcaggg ccccagcaag 240
aaggcagcca agcacaaggc agctgaggtg gccctcaaac acctcaaagg ggggagcatg 300
ctggagccgg ccctggagga cagcagttct tttttctcccc tagactcttc actgcctgag 360
gacattccgg ttttactgc tgcagcagct gctaccccag ttccatctgt agtcctaacc 420
aggagccccc ccatggaact gcagcccctt gtctcccctc agcagtctga gtgcaacccc 480
gttggtgctc tgcaggagct ggtggtgcag aaaggctggc ggttgccgga gtacacagtg 540
acccaggagt ctgggccagc ccaccgcaaa gaattcacca tgacctgtcg agtggagcgt 600
ttcattgaga ttgggagtgg cacttccaaa aaattggcaa agcggaatgc ggcggccaaa 660
atgctgcttc gagtgcacac ggtgcctctg gatgcccggg atggcaatga ggtggagcct 720
gatgatgacc acttctccat tggtgtgggc ttccgcctgg atggtcttcg aaaccggggc 780
ccaggttgca cctgggattc tctacgaaat tcagtaggag agaagatcct gtcctccgc 840
agttgctccc tgggctccct gggtgccctg ggccctgcct gctgccgtgt cctcagtgag 900
ctctctgagg agcaggcctt tcacgtcagc tacctggata ttgaggagct gagcctgagt 960
ggactctgcc agtgcctggt ggaactgtcc acccagccgg ccactgtgtg tcatggctct 1020
gcaaccacca gggaggcagc ccgtggtgag gctgcccgcc gtgccctgca gtacctcaag 1080
atcatggcag gcagcaagtg a 1101

<210> 140
<211> 219
<212> DNA
<213> Human immunodeficiency virus

<300>
<302> TAT (HIV)
<310> U44023

<400> 140
atggagccag tagatcctag cctagagccc tggaagcatc caggaagtca gcctaagact 60
gcttgtacca cttgctattg taaagagtgt tgcttttcatt gccaagtttg tttcataaca 120
aaaggcttag gcatctccta tggcaggaag aagcggagac agcgacgaag aactcctcaa 180
ggtcatcaga ctaatcaagt ttctctatca aagcagtaa 219

<210> 141
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand
(R1A) of a dsRNA that is homologous to an MDR1 sequence

<400> 141
ccaucucgaa aagaaguuaa ga 22

<210> 142
<211> 24
<212> RNA

<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand (R1B) of a dsRNA, that it
complementary to an MDR1 sequence

<400> 142
ucuuaacuuc uuuucgagau gggu 24

<210> 143
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand
(R2A) of a dsRNA that is homologous to an MDR1 sequence

<400> 143
uauagguucc aggcuugcug ua 22

<210> 144
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand
(R3A) of a dsRNA that is homologous to an MDR1 sequence

<400> 144
ccagagaagg ccgcaccugc au 22

<210> 145
<211> 24
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand (R3B) of a dsRNA, that it
complementary to an MDR1 sequence

<400> 145
augcaggugc ggccuucucu ggcu 24

<210> 146
<211> 21
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand
(R4A) of a dsRNA that is homologous to an MDR1 sequence

<400> 146
ccaucucgaa aagaaguuaa g 21

<210> 147
<211> 21
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand (R4B) of a dsRNA, that it
complementary to an MDR1 sequence

<400> 147
uaacuucuuu ucgagauggg u 21

<210> 148
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand
(S1A) of a dsRNA, that is homologous to the YFP- and
GFP sequence, respectively

<400> 148
ccacaugaag cagcacgacu uc 22

<210> 149
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand(S1B) of a dsRNA that is
complementary to the YFP- and GFP sequence, respectively

<400> 149
gaagucgugc ugcuucaugu gg 22

<210> 150
<211> 21
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand(S7A) of a dsRNA that is homologous
to the YFP- and GFP sequence, respectively

<400> 150
ccacaugaag cagcacgacu u 21

<210> 151
<211> 21
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand(S7B) of a dsRNA, that is
complementary to the YFP- and GFP sequence, respectively

<400> 151
gucgugcugc uucauguggu c 21

<210> 152
<211> 24
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand(R2B) of a dsRNA that is
complementary to the MDR-1 sequence

<400> 152
uacagcaagc cuggaaccua uagc 24

<210> 153
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand
(K1A) of a dsRNA that is homologous to the 5'-UTR of
the neomycin sequence

<400> 153
acaggaugag gaucguuucg ca 22

<210> 154
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand(K1B) of a dsRNA that is
complementary to the 5'-UTR of the neomycin sequence

<400> 154
ugcgaaacga uccucauccu gu 22

<210> 155
<211> 21
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand
(K3A) of a dsRNA that is homologous to the 5'-UTR of the
neomycin sequence

<400> 155
gaugaggauc guuucgcaug a 21

<210> 156
<211> 21
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand(K3B) of a dsRNA that
complementary to the 5'-UTR of the neomycin sequence

<400> 156
augcgaaacg auccucaucc u 21

<210> 157
<211> 24
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand
(K2A) of a dsRNA that is homologous to the 5'-UTR of the
neomycin sequence

<400> 157
acaggaugag gaucguuucg caug 24

<210> 158
<211> 24
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand(K2B) of a dsRNA that is
complementary to the 5'-UTR of the neomycin sequence

<400> 158
ugcgaaacga uccucauccu gucu 24

<210> 159
<211> 24
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence:
antisense strand(S4B) of a dsRNA that is

complementary to the YFP- and GFP sequence, respectively

<400> 159
gaagucgugc ugcuucaugu gguc 24

<210> 160
<211> 24
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand (PKC1 A) of a dsRNA that is homologous to the proteinkinase C sequence

<400> 160
cuucuccgcc ucacaccgcu gcaa 24

<210> 161
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: antisense strand(PKC2 B) of a dsRNA that is complementary to the proteinkinase C sequence

<400> 161
gcagcggugu gaggcggaga ag 22

<210> 162
<211> 21
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: antisense strand(S12B) of a dsRNA that is complementary to the YFP- and GFP sequence, respectively

<400> 162
aagucgugcu gcuucaugug g 21

<210> 163
<211> 23
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: antisense strand(S11B) of a dsRNA that is complementary to the YFP- and GFP sequence, respectively

<400> 163
aagucgugcu gcuucaugug guc 23

<210> 164
<211> 20
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand (S13A) of a dsRNA that is homologous to the YFP- and GFP sequence, respectively

<400> 164
ccacaugaag cagcacgacu 20

<210> 165
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: antisense strand(S13B) of a dsRNA that is complementary to the YFP- and GFP sequence, respectively

<400> 165
agucgugcug cuucaugugg uc 22

<210> 166
<211> 20
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: antisense strand(S14B) of a dsRNA that is complementary to the YFP- and GFP sequence, respectively

<400> 166
agucgugcug cuucaugugg 20

<210> 167
<211> 24
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand (S4A) of a dsRNA that is homologous to the YFP- and GFP sequence, respectively

<400> 167
ccacaugaag cagcacgacu ucuu 24

<210> 168
<211> 21

<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand (ES-7A) of a dsRNA that is homologous to the human EGFR sequence

<400> 168
aacaccgcag caugucaaga u 21

<210> 169
<211> 21
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: antisense strand(ES-7B) of a dsRNA that is complementary to the human EGFR sequence

<400> 169
cuugacaugc ugcgguguuu u 21

<210> 170
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: sense strand (ES-8A) of a dsRNA that is homologous to the human EGFR sequence

<400> 170
aaguuaaaau ucccgucgcu au 22

<210> 171
<211> 22
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: antisense strand(ES-8B) of a dsRNA that is complementary to the human EGFR sequence

<400> 171
ugauagcgac gggaauuuua ac 22

<210> 172
<211> 22
<212> RNA
<213> Synthetic sequence

<220>

<223> Description of the synthetic sequence: sense strand (ES-2A) of a dsRNA that is homologous to the human EGFR sequence

<400> 172
agugugaucc aagcuguccc aa 22

<210> 173
<211> 24
<212> RNA
<213> Synthetic sequence

<220>
<223> Description of the synthetic sequence: antisense strand(ES-5B) of a dsRNA that is complementary to the human EGFR sequence

<400> 173
uugggacagc uuggaucaca cuuu

Fig. 1a

Fig. 1b

Fig. 2

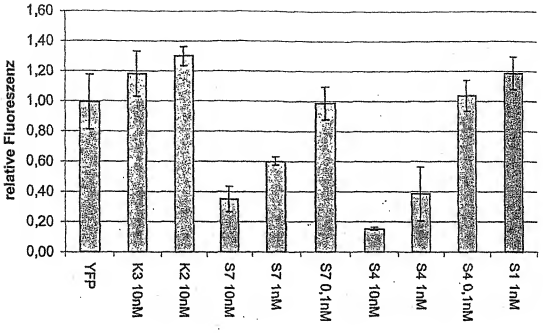

relative Fluoreszenz
1,60
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
YFP
K3 10nM
K2 10nM
S7 10nM
S7 1nM
S7 0,1nM
S4 10nM
S4 1nM
S4 0,1nM
S1 1nM

Fig. 3

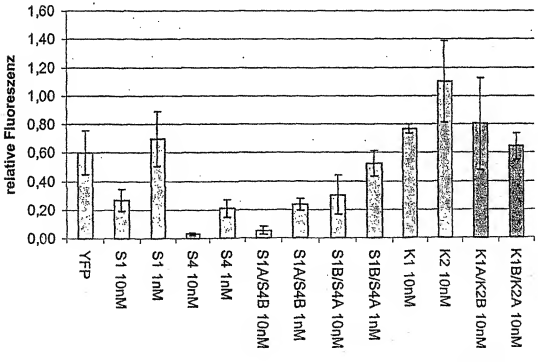

relative Fluoreszenz
1,60
1,40
1,20
1,00
0,80
0,60
0,40
0,20
0,00
YFP
S1 10nM
S1 1nM
S4 10nM
S4 1nM
S1A/S4B 10nM
S1A/S4B 1nM
S1B/S4A 10nM
S1B/S4A 1nM
K1 10nM
K2 10nM
K1A/K2B 10nM
K1B/K2A 10nM

Fig. 4

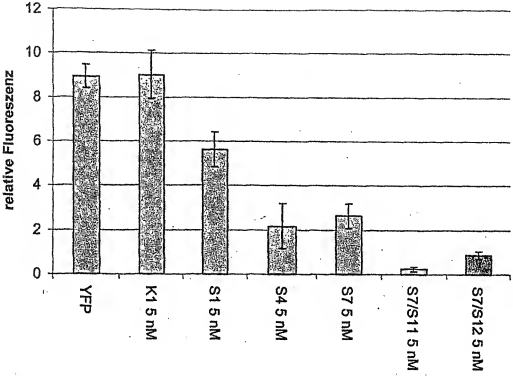

relative Fluoreszenz
12
10
8
6
4
2
0
YFP
K1 5 nM
S1 5 nM
S4 5 nM
S7 5 nM
S7/S11 5 nM
S7/S12 5 nM

Fig. 5

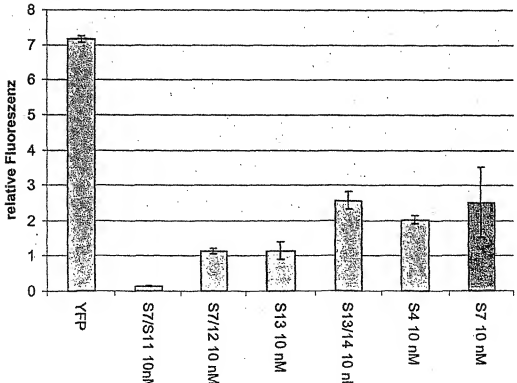

relative Fluoreszenz
8
7
6
5
4
3
2
1
0
YFP
S7/S11 10nM
S7/12 10 nM
S13 10 nM
S13/14 10 nM
S4 10 nM
S7 10 nM

Fig. 6

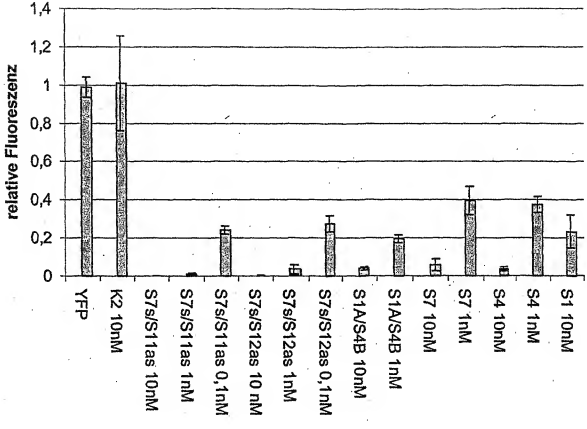

relative Fluoreszenz
1,4
1,2
1
0,8
0,6
0,4
0,2
0
YFP
K2 10nM
S7s/S11as 10nM
S7s/S11as 1nM
S7s/S11as 0,1nM
S7s/S12as 10 nM
S7s/S12as 1nM
S7s/S12as 0,1nM
S1A/S4B 10nM
S1A/S4B 1nM
S7 10nM
S7 1nM
S4 10nM
S4 1nM
S1 10nM

Fig. 7

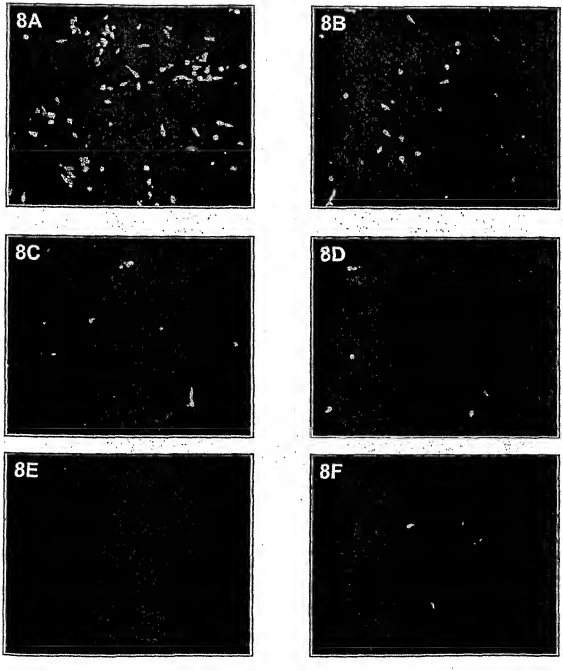


Fig. 8

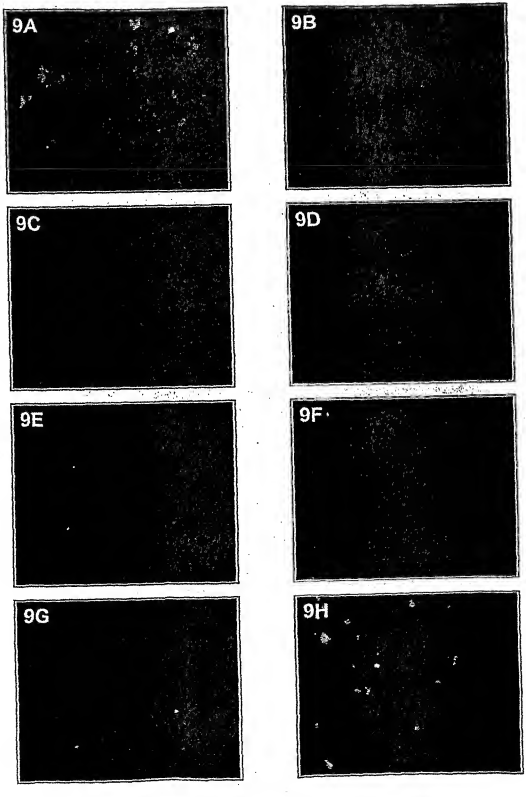


Fig. 9

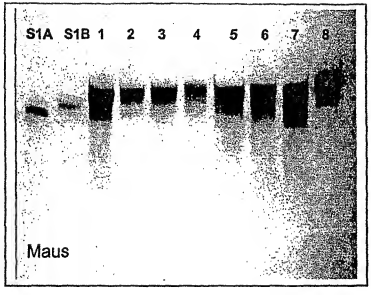


Fig. 10

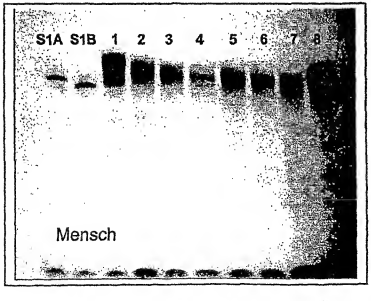


Fig. 11

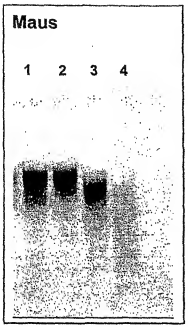


Fig. 12

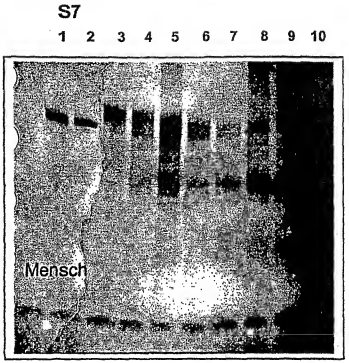


Fig. 13

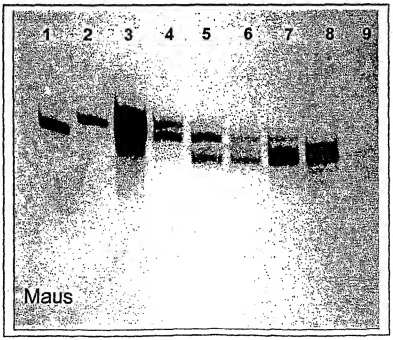


Fig. 14

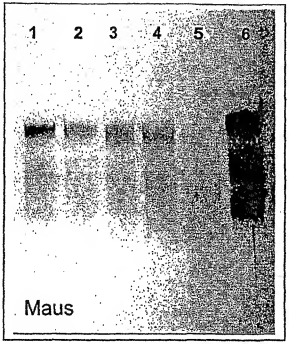


Fig. 15

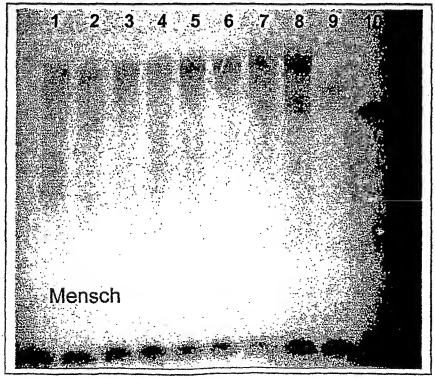


Fig. 16

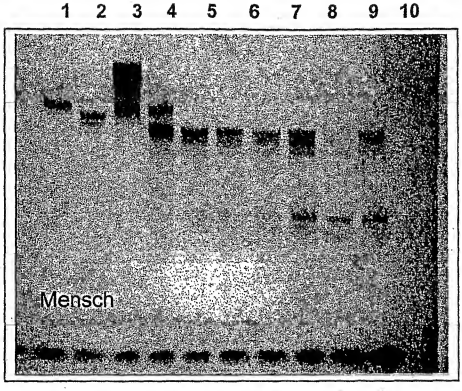


Fig. 17

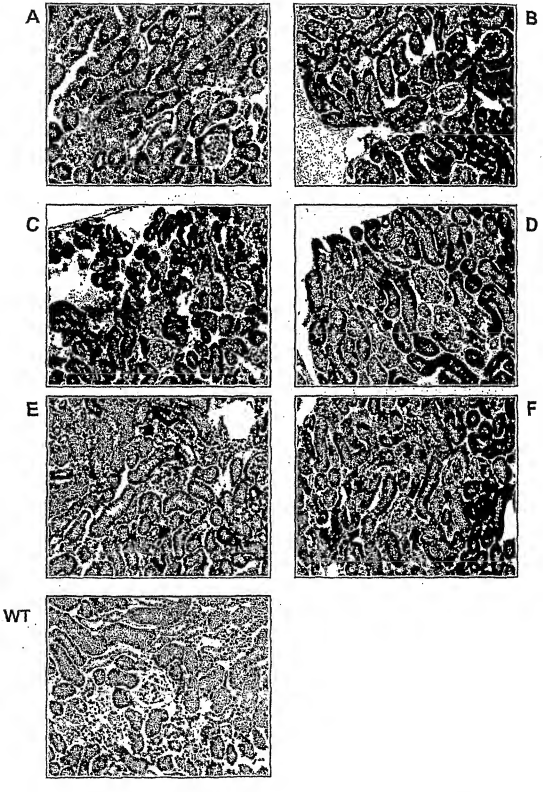


Fig. 18

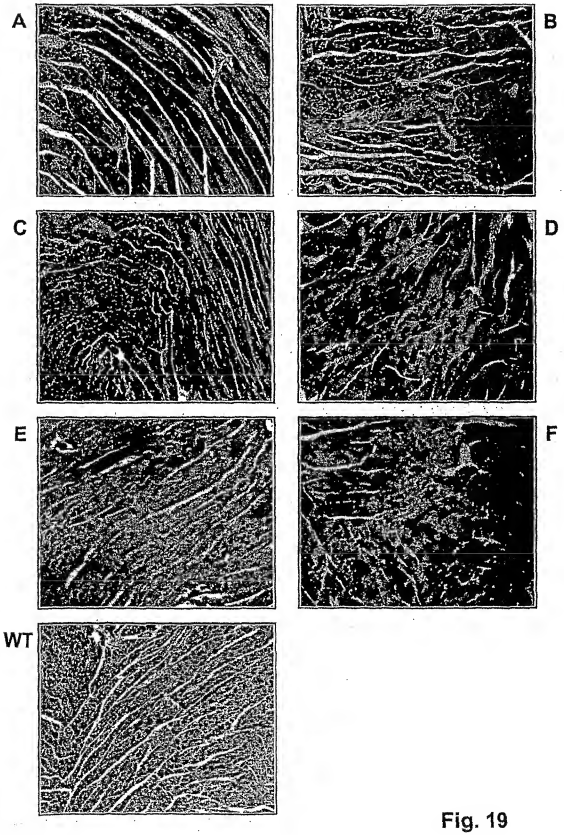


Fig. 19

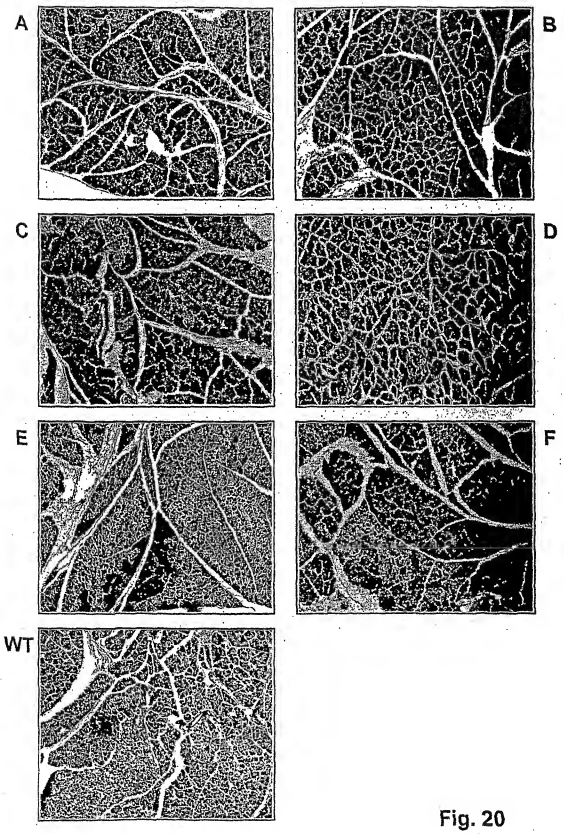


Fig. 20

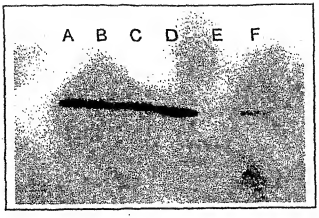


Fig. 21

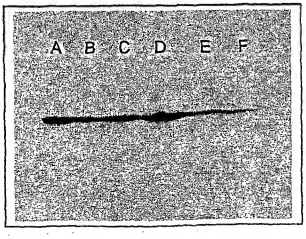


Fig. 22

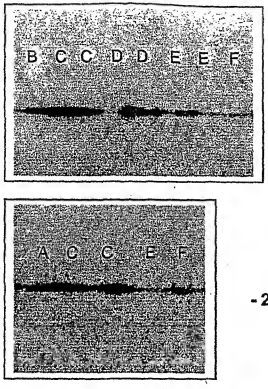

B C C D D E E F
- 26 kDa
A C C E F
- 26 kDa

Fig. 23

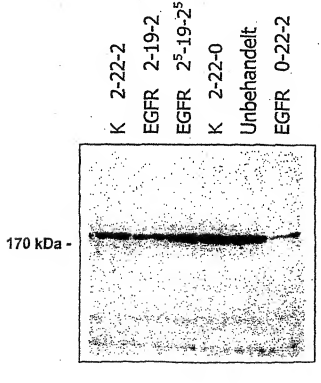

K 2-22-2
EGFR 2-19-2
EGFR 2⁵-19-2⁵
K 2-22-0
Unbehandelt
EGFR 0-22-2
170 kDa -

Fig. 24

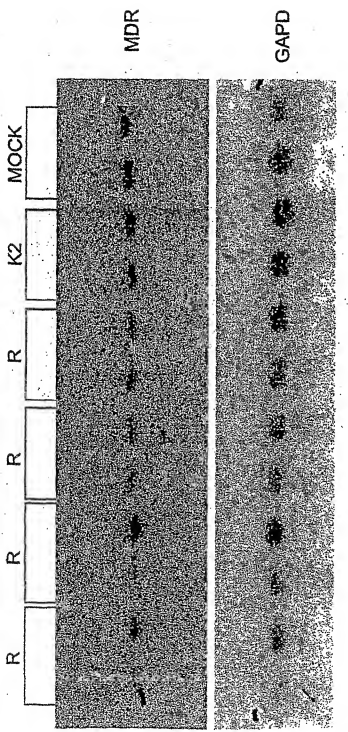


Fig. 25a

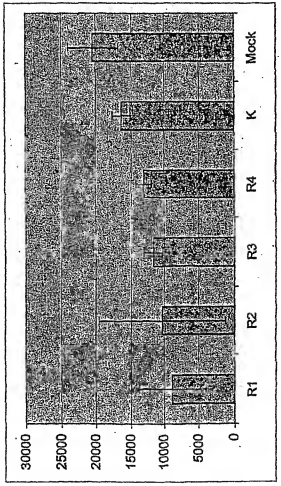


Fig. 25b

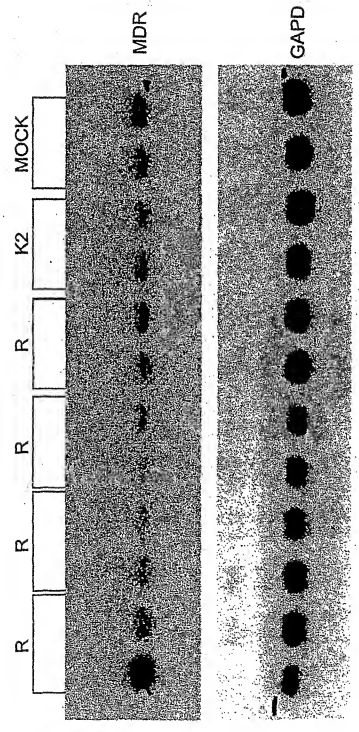


Fig. 26a

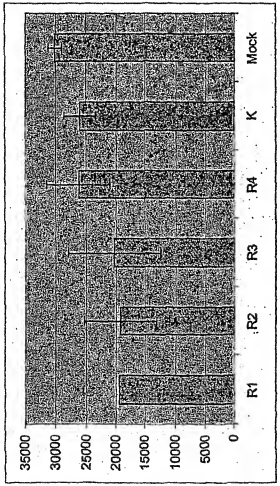
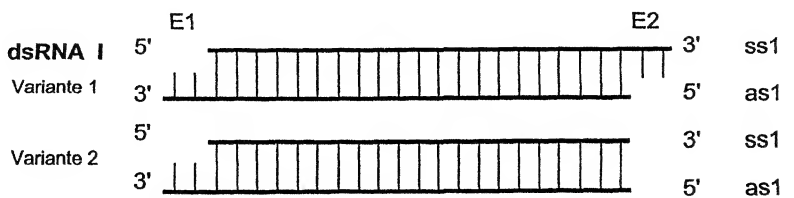


Fig. 26b


175 nM
Hellfeld
Fluoreszenz
MOCK-Transfektion
Hellfeld
Fluoreszenz

Fig. 27


E1
E2
dsRNA I
5'
3'
ss1
Variante 1
3'
5'
as1
5'
3'
ss1
Variante 2
3'
5'
as1